PATCH TESTING TO DETECT CONTACT HYPERSENSITIVITY TO CORTICOSTEROIDS

Dissertation Submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In fulfilment of the regulations for the award of the degree

M.D.

DERMATOLOGY, VENEREOLOGY AND LEPROLOGY

DEPARTMENT OF DERMATOLOGY, VENEROLOGY AND LEPROLOGY

PSG INSTITUTE OF MEDICAL SCIENCE AND RESEARCH
THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY
CHENNAI, TAMILNADU

APRIL 2016

PATCH TESTING TO DETECT CONTACT HYPERSENSITIVITY TO CORTICOSTEROIDS

In fulfilment of the regulations for the award of the degree

M.D.

DERMATOLOGY, VENEREOLOGY AND LEPROLOGY

GUIDE

DR. C.R. SRINIVAS, MD
DEPARTMENT OF DERMATOLOGY,
VENEREOLOGY AND LEPROLOGY

PSG INSTITUTE OF MEDICAL SCIENCE AND RESEARCH
THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY
CHENNAI, TAMILNADU

APRIL 2016

CERTIFICATE

This is certify that the thesis entitled **"PATCH TESTING TO DETECT CONTACT HYPERSENSITIVITY TO CORTICOSTEROIDS"** is a bonafide work of **DR. AKILA K.** done under the direct guidance and supervision of **DR. C.R. SRINIVAS, MD,** in the department of Dermatology, Venereology and Leprology, PSG Institute of Medical Sciences and Research, Coimbatore in fulfillment of the regulations of Dr.MGR Medical University for the award of MD degree in Dermatology, Venereology and Leprology.

DR. C. R. SRINIVAS
Professor & Head of Dept.
Dept. of DVL

DR.RAMALINGAM
DEAN

DECLARATION

I hereby declare that this dissertation entitled **"PATCH TESTING TO DETECT CONTACT HYPERSENSITIVITY TO CORTICOSTEROIDS "** was prepared by me under the direct guidance and supervision of **DR. C.R. SRINIVAS, MD,** PSG Institute of Medical Sciences and Research, Coimbatore.

The dissertation is submitted to the Tamilnadu Dr.MGR Medical University in fulfillment of the University regulation for the award of MD degree in Dermatology, Venereology and Leprology. This dissertation has not been submitted for the award of any other Degree or Diploma.

DR. AKILA K.

CERTIFICATE BY THE GUIDE

This is certify that the thesis entitled **"PATCH TESTING TO DETECT CONTACT HYPERSENSITIVITY TO CORTICOSTEROIDS"** is a bonafide work of **DR. AKILA K.** done under my direct guidance and supervision in the department of Dermatology, Venereology and Leprology, PSG Institute of Medical Sciences and Research, Coimbatore in fulfillment of the regulations of Dr.MGR Medical University for the award of MD degree in Dermatology, Venereology and Leprology.

DR. C.R. SRINIVAS
Professor
Dept. of DVL

ACKNOWLEDGEMENT

On the very outset, I express my sincere gratitude to Dr.C.R.Srinivas who had guided me from scratch till the last minute. I thank him for giving me this opportunity and kindling me to go into every detail involved in regard to this study “Patch testing to detect contact hypersensitivity to corticosteroids.” I thank him for being an example as to how every student reason out everything.

I am grateful to Dr. Reena Rai who had constantly contemplated the progress of my post graduation and my dissertation and for all her driving force and knowledge she imparted on us.

I thank Dr. Surendran and Dr. Mahadevan for their enlightening thoughts towards clinical and therapeutics.

I express my thanks to Dr. Chemboli Lakshmi for her contributions.

I thank Dr. Shanmuga Sekar and Dr. Karthiga for their guidance regarding certain practical issues in respect to the study.

I also thank Dr.Sornakumar, Dr. Kumaresan, Dr.Pradeep, Dr.Kavitha,Dr.Deepak and Dr.Priya for their support in completion of my thesis.

I wish to express my gratitiudes towards my fellow juniors and seniors who contributed their time and efforts.

I thank all our staff including Mr.Thirumoorthy, technician and Mrs.Shanti for their endeavours.

I also place a sincere note of appreciation to the patients who contributed their efforts towards the success of this tedious study

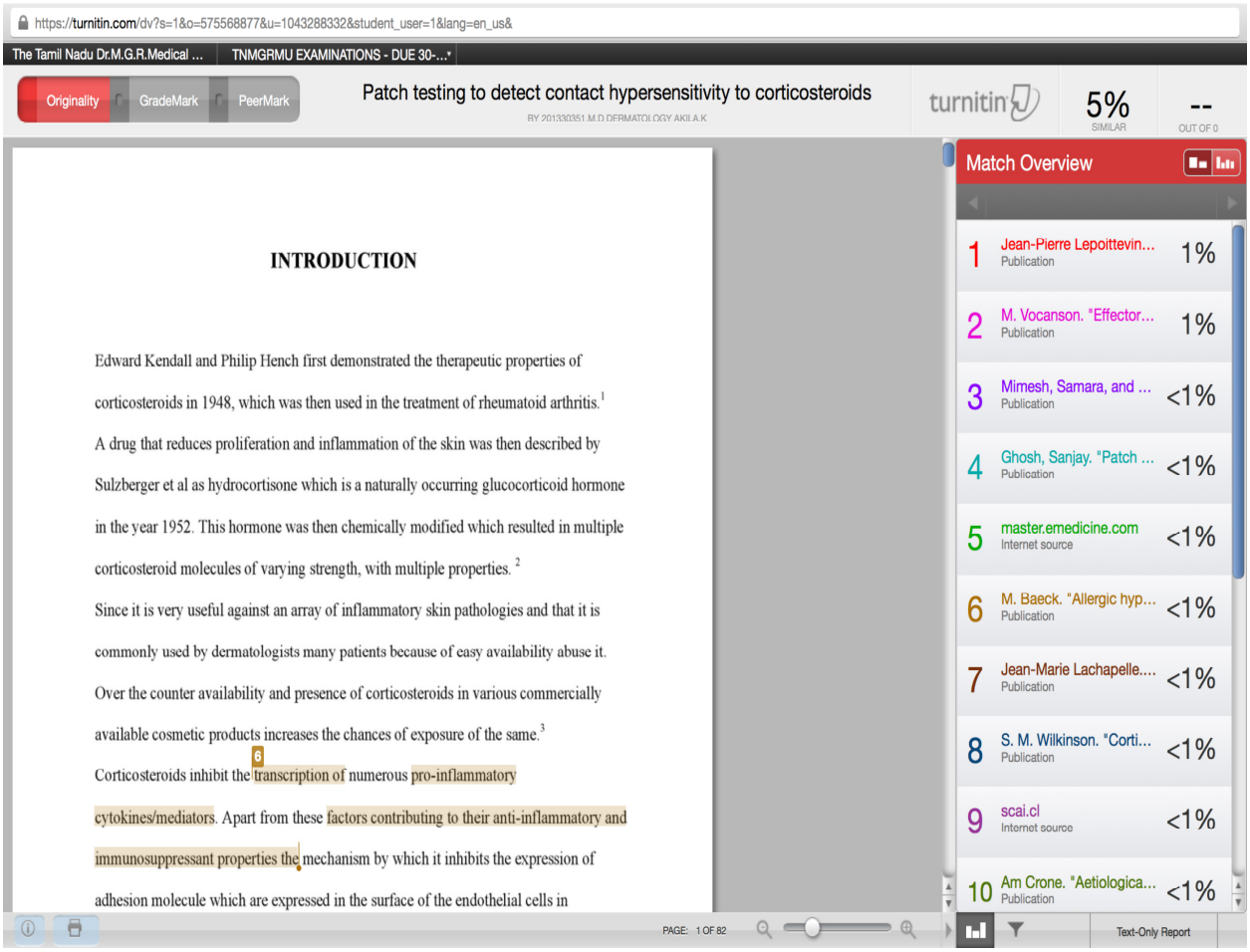
I wholeheartedly thank my dear colleagues Dr.Manu Vidhya, Dr.Anita, Dr.Revathi for their constant support and co-operation throughout the study.

I express all my love and gratitude towards my family – my father, mother, brother, sister in law, lovely daughter Sangamithra, cute little Kavya and last but never the least my husband for being by my side in all hardships and happiness throughout my postgraduation course and dissertation

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES


https://turnitin.com/dv?s=1&o=575568877&u=1043288332&student_user=1&lang=en_us&
The Tamil Nadu Dr.M.G.R.Medical ...
TNMGRMU EXAMINATIONS - DUE 30-...
Originality
GradeMark
PeerMark
Patch testing to detect contact hypersensitivity to corticosteroids
turnitin
5%
SIMILAR
--
OUT OF 0
INTRODUCTION
Edward Kendall and Philip Hench first demonstrated the therapeutic properties of corticosteroids in 1948, which was then used in the treatment of rheumatoid arthritis.[1]
A drug that reduces proliferation and inflammation of the skin was then described by Sulzberger et al as hydrocortisone which is a naturally occurring glucocorticoid hormone in the year 1952. This hormone was then chemically modified which resulted in multiple corticosteroid molecules of varying strength, with multiple properties.[2]
Since it is very useful against an array of inflammatory skin pathologies and that it is commonly used by dermatologists many patients because of easy availability abuse it.
Over the counter availability and presence of corticosteroids in various commercially available cosmetic products increases the chances of exposure of the same.[3]
Corticosteroids inhibit the transcription of numerous pro-inflammatory cytokines/mediators. Apart from these factors contributing to their anti-inflammatory and immunosuppressant properties the mechanism by which it inhibits the expression of adhesion molecule which are expressed in the surface of the endothelial cells in
PAGE: 1 OF 82
Match Overview
1 Jean-Pierre Lepoittevin... Publication 1%
2 M. Vocanson. "Effector... Publication 1%
3 Mimesh, Samara, and ... Publication <1%
4 Ghosh, Sanjay. "Patch ... Publication <1%
5 master.emedicine.com Internet source <1%
6 M. Baeck. "Allergic hyp... Publication <1%
7 Jean-Marie Lachapelle.... Publication <1%
8 S. M. Wilkinson. "Corti... Publication <1%
9 scai.cl Internet source <1%
10 Am Crone. "Aetiologica... Publication <1%
Text-Only Report

PATCH TESTING TO DETECT CONTACT HYPERSENSITIVITY TO CORTICOSTEROIDS

Introduction:

Topical corticosteroids are extensively used preparations as prescription medicines and as over the counter medications in a wide variety of inflammatory dermatosis. These are increasingly recognized as a cause of allergic contact dermatitis. The incidence of which is reported to be 0.5 – 5% in various studies in Europe and USA. Studies in South East Asia show a prevalence of 3.29% in Thailand. But there are limited data available in India and no studies determining the same. The subtle clinical presentations are responsible for missing this condition by the practicing doctors. One should thus consider this diagnosis when there is worsening or poor response of the existing dermatosis to topical steroids.

Objectives:

To study the contact hypersensitivity by patch testing in patients who do not respond to or aggravate after using topical corticosteroids.

Materials and Methods:

24 patients aged 14 to 82 years with 17 males and 7 females underwent corticosteroid patch testing with chemotechnique series which had 9 corticosteroid allergens including control – petrolatum and patients own products which they were applying recently. Reading was taken on Day3, 5 and 7 and results interpreted according to ICDRG scale.

Results:

4 out of 24 patients (16.3% positivity) tested positive to the allergens in the corticosteroid series and 1 tested positive patients own medication.

Conclusion:

On reviewing the details of the positive outcomes- They were single positivity's except in one patient with reaction of two different groups of steroids – tixocortol of Group A in the series and Flutivate ointment (Fluticasone) in her own medications. The other patterns that were observed were that the patients included in the study had longer duration of dermatosis, hence long term application of steroids. The primary diagnosis for which topical steroid most commonly used was Atopic dermatosis followed by stasis dermatitis and allergic contact dermatitis. Thus, patch testing in patients suspected with corticosteroid hypersensitivity will help in directing therapy.

INTRODUCTION

Edward Kendall and Philip Hench first demonstrated the therapeutic properties of corticosteroids in 1948, which was then used in the treatment of rheumatoid arthritis.[1]

A drug that reduces proliferation and inflammation of the skin was then described by Sulzberger et al as hydrocortisone which is a naturally occurring glucocorticoid hormone in the year 1952. This hormone was then chemically modified which resulted in multiple corticosteroid molecules of varying strength, with multiple properties. [2]

Since it is very useful against an array of inflammatory skin pathologies and that it is commonly used by dermatologists many patients because of easy availability abuse it. Over the counter availability and presence of corticosteroids in various commercially available cosmetic products increases the chances of exposure of the same.[3]

Corticosteroids inhibit the transcription of numerous pro-inflammatory cytokines/mediators. Apart from these factors contributing to their anti-inflammatory and immunosuppressant properties the mechanism by which it inhibits the expression of adhesion molecule which are expressed in the surface of the endothelial cells in inflammation and causes apoptosis of basophils.[4]

It can thus be explained that the corticosteroids which has potent anti-inflammatory agents and immunomodulators used in the treatment of allergic manifestations (in the broad sense) are capable of producing contact sensitization is thus paradoxical.[5]

These contact hypersensitivity reactions were first described in the 1950's, which was following topical and parenteral hydrocortisone.[6]

Allergic contact dermatitis is an inflammatory skin reaction to direct contact with any substance that a person is previously sensitized. It occurs in two phases.

1. Sensitization phase – where immune system is primed to an allergen.
2. Second – elicitation of the allergy - a Type IV delayed hypersensitivity reaction in which a cell-mediated allergic response is triggered.[7]

To develop contact hypersensitivity to any drug it requires prior exposure of the same to which antibodies are produced – either of the IgG or the IgE type and involves either CD4 or more commonly a CD8 type of T cell proliferation.[8]

As we discussed earlier there exists a huge array of corticosteroid molecules against innumerable indications and thus used both topical and parenteral. Although systemic sensitization is documented topical is by far the commonest.[9]

Apart from these, intranasal and inhalations routes of sensitization are also noted.[10] Understanding the properties of corticosteroids is also important to understand the mechanism of allergic contact dermatitis. This includes the various groups, their potencies, the preparation and vehicle on dispensing the drug.

The corticosteroid potency is classified upon the vasoconstrictive properties from mild to high potent ones, which are used depending upon the severity and the nature of the disease.[11]

Cutaneous side effects of topical corticosteroidsinclude skin atrophy – epidermis and dermis- resulting in hypopigmentation, acne, telengiectsia, striae etc. These thus limit the long term application. Apart from this because of the atrophy especially in intertriginous areas, face- it increases the penetration of allergens.

Sensitization to topical steroids are increasingly documented in association with those diseases which demands long term applications- most commonly noted in atopic dermatitis, stasis dermatitis, hand and foot eczema etc., It could also be explained by the fact that in these conditions due to impaired skin barrier functions there is enhanced penetration of the allergens. Also, the local pro-inflammatory (thus availability of Antigen presenting cell's –LC's) environment favours antigen presentation.[8]

The incidence of allergic contact dermatitis following topical application varies from 0.5 to 5%[4,11-13]

Only limited data are available of the prevalence and patterns of corticosteroid hypersensitivity in Asia. A study in Thailand estimated allergic contact dermatitis to corticosteroids to be 3.29%.[110]

In India no studies have been published regarding the same.[3]

The clinical features of contact hypersensitivity to corticosteroids are very subtle and hence easily missed.[8] Any patient with chronic skin disease with topical steroid application has poor or no response, or worsening of symptoms on application of topical corticosteroids must thus be patch tested.[13]

Understanding the properties of corticosteroid molecules- its topical bio-availability, the concentration and the vehicle that is optimal for patch testing is debatable.

Same is applicable regarding the readings – delayed reading should be advocated owing to its pharmacological- anti-inflammatory properties. Day 5 and Day 7 readings are thus recommened.[7]

Apart from the panel of allergen patients own medications has to be patch tested because it could only explain the factors present in the preparation that

might enhance the penetration-vehicles, excipients- preservatives, and package itself (nickel).

Interpretation of patch test results again is also peculiar in case of corticosteroids[8]

- False positives and false negatives owing to its vasodilation and vasoconstriction properties.[8]
- Edge effect in corticosteroids- thin rim of erythema because of the anti inflammatory effect at the site of patch testing and dilution of concentration in periphery has to be considered positive in case of corticosteroid patch testing.[14]

NEED FOR STUDY

Hence our study was undertaken to determine the prevalence of contact hypersensitivity to topical corticosteroids among patients who had used it for a prolonged duration without significant improvement or among cases that worsened following the use of topical corticosteroid preparations.

AIM OF THE STUDY

PRIMARY AIM

- To study the contact hypersensitivity of patients to topical steroids who do not respond to or aggravate after using topical corticosteroids

SECONDARY AIMS

- To determine the prevalence in regard to the contact hypersensitivity to topical steroids in suspectedpts attending our OPD

- To find and to recommend the use of suitable topical corticosteroid preparations devoid of the allergen and/or the allergen that may cross react

REVIEW OF LITERATURE

Skin being the outermost barrier of our body, is the first to encounter numerous substances from the environment, thus being exposed to various physical, chemical, and biological products that may give rise eczema.[107]

Eczema (to boil) presents clinically as erythema, hyperpigmentation, scaling, vesicles with exudation.[17] This can be

1. Acute eczema- causing pink erythema and scaling with exudation.
2. Subacute
3. Chronic - lichenification

Eczema that is caused by exogenous agents which thus come in contact or penetrate the skin to produce inflammation is termed as contact eczema.[15]

Allergic contact dermatitis is thus defined as an inflammatory skin reaction to direct contact with noxious agents present in the environment.[16] However, not all allergens are noxious.

Contact dermatitis can be caused by

- Irritant materials resulting in irritant contact dermatitis resulting from acids and alkalis.[7]or
- Allergens resulting in allergic contact dermatitis.

Allergic contact dermatitis occurs as a specific immune response against the contactant to which the patient is previously sensitized. And the immune reaction, which is generated against the antigen, causes tissue damage. [17]

Allergic contact dermatitis/Contact hypersensitivity/contact sensitivity are all considered as synonymous terms.[15]

Contact hypersensitivity occurs as a result of delayed hypersensitivity (DTH) reaction – which can be reproduced by direct contact of skin with the offending chemical in a person who is previously exposed to or sensitized to the same chemical.[15] The site thus becomes erythematous, vesicular or scaly.

A succession of physicochemical processes occur that can be didactically divided into 2 phases all of which involves the immune system

1) Sensitization phase – In which, the immune system is primed to an allergen.
2) Elicitation of the allergy/challenge/efferent phase - a Type IV DTH in which, a cell-mediated allergic response is triggered.[18]

These are best understood with the help of this picture:

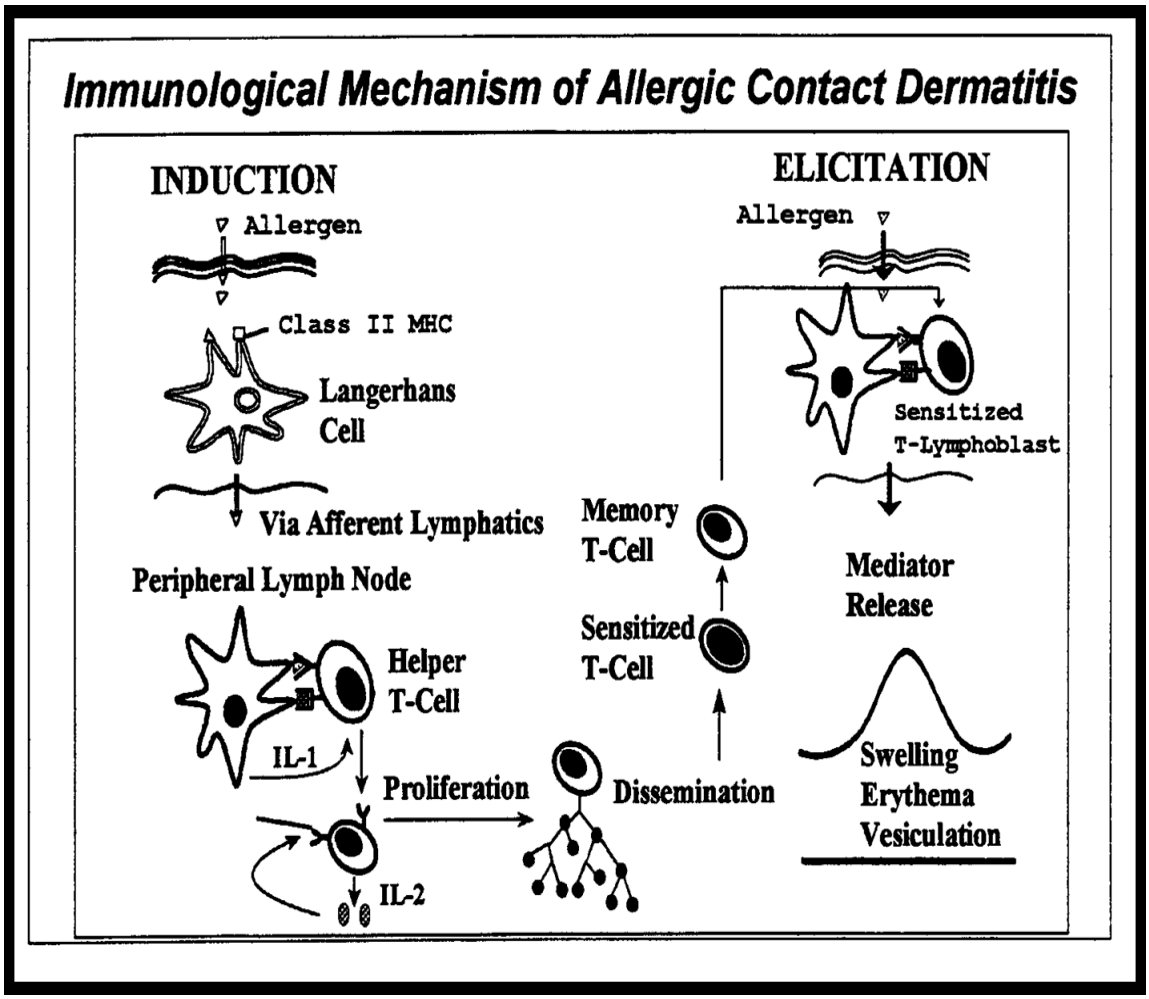


Figure - 1

The understanding of which is as follows:

Three elements are required for a **contact hypersensitivity reaction** to take place which includes

1. Antigen presenting cells or Langerhans/ dendritic cells (DC),
2. Haptenspecific T-cells,
3. Haptens.[15]

Table – 1

PROCESSES INVOLVED IN ALLERGIC CONTACT DERMATITIS

Haptens are of low molecular weight (<500 Daltons) which are nothing but the contact allergen that is responsible for causing allergic contact dermatitis. Not immunogenic on their own and need to bind to epidermal proteins.

The physical and chemical properties of the haptens allow these to cross the stratum corneum[106]

↓

They form **hapten-protein conjugates** on coming in contact with the epidermis.

Thus making it a complete antigen and hence protein reactive.

This conjugate is a result of covalent binding to certain amino acids of protein carriers present in skin.

The covalent binding is the result of interaction of nucleophilic–electrophilic reactions between chemicals and some amino acids, such as cysteine

↓

These conjugates are recognized as a foreign body by the **Langerhan cells** or the dendritic cells (DCs), These then internalizes the protein

↓

Langerhan cells are transported to the lymph nodes

There they transform into **dendritic cells** by differentiation, which are immune – stimulatory in nature

↓

Enter the lymph glands and present the allergenic epitope associated with the allergen to the **T lymphocytes**.

These processes are controlled by TNF-α and few IL-1, 13 and 18 which are cytokines and chemokines– that either promote or inhibit the mobilization and migration of these LCs.

↓

These T lymphocytes then clonally multiply after differentiation resulting in **Memory T cells.**

Thus if the same sensitized individual is exposed to the same allergen, these T lymphocytes will respond more quickly and aggressively, giving rise to the various manifestations of allergic contact dermatitis.[18]

Sensitisation phase lasts upto 10-15 days in man

Elicitaion phase occurs as quickly as 24 hours.[15]

White et al. (1986) hypothesized that there is a threshold to this event of sensitization by allergens. And depends upon the extent to which induces the up-regulation of the required cytokines and inflammatory mediators.

The vehicle in which the allergen reaches the skin also determines the sensitisation of the epidermis by augumenting the percutaneous penetration hence influx of cytokines.[18]

MEMORY RESPONSE

Upon sensitization to chemical that causes allergy, future contacts with the same substance can trigger a reaction, in the original site of sensitization – referred to as a memory response. Thus progressing directly to elicitation phase of allergic contact dermatitis.[17]

At the end of sensitization phase, memory T cells which have been activated the binding are found in theblood and in the skin (peripheral memory cells) and in the Lymph nodes- called as central. The skin though appears normal these memory T cells will be activated directly in the skin and excessively brought to the site if it comes in contact again.[18]

For example,

If a person has an allergic contact dermatitis due to nickel strap, touching the contact allergen present in coins, handles etc., can trigger an allergic reaction on the primary site.

This is a result of the memory T-lymphocytes, which remain in the skin of primary contact. This Memory response, or "Retest Reactivity", occurs in about 2 to 3 days after contact, and can be present for 2 to 4 weeks.

Thus in a person who is already sensitized with the same allergen the response is as early as 24 to 96 hours after contact with the causative allergen.[15-18]

REGULATION OF CONTACT SENSITIVITY

Initially it was hypothesis that few days following hapten presentation there is down-regulation of the contact hypersensitivity due to removal of the allergen from the skin by body. [106]

Although, there are reports that suggest that the allergens could say in the skin – epidermis for even more than 2 weeks after an application. There are reports where they have observed that ultraviolet radiation induced allergic contact dermatitis patients had persistence of ketoprofene in the skin for as long as years.

There are numerous mechanisms that involve in suppression of the regulatory mechanisms which are involved in the inflammation and hence limit tissue damage.

Which include the following [102]

(i) the clearance of bound antigen by effector T lymphocytes

(ii) recruitment of cytokines involves in the antagonizing action against inflammation

(iii) binding of non MHC ligands (likecadherins, PD-L1, RANK-L, etc.) for inhibitory immune receptors

(iv) upregulation of T regulatory cells which down regulates these mechanisms.

FUTURE PROSPECTIVES

Allergic contact dermatitis, is thus known to be mediated by T Lymphocytes of CD8 origin.

There are ongoing studies that in molecular levels observe the binding of haptens, skin recruitment of CD8 T lymphocytes and the cellular networks involved in the same.[17]

Epicutaneous exposure to sensitizing chemicals activates thus recruits many inflammatory mediators and inflammatory pathways.

Hence these are potential targets for detailed research and development of newer medications that attend to these mechanisms. Modalities that can somehow cause tolerance to these haptens in patients with contact sensitization are potential targets, but will need a detailed chemical and molecularstudies.[18]

DIAGNOSIS OF ALLERGIC CONTACT DERMATITIS

History

Detailed history plays a crucial role in the diagnosis in regard to the duration, where and how it started and coincidence to any contact / topical applications.[7]

Physical examination

The distribution of dermatitis, in relation to the severity of the disease which usually correlates with the contact of the allergen. This is crucial for the diagnosis of allergic contact dermatitis.[7]

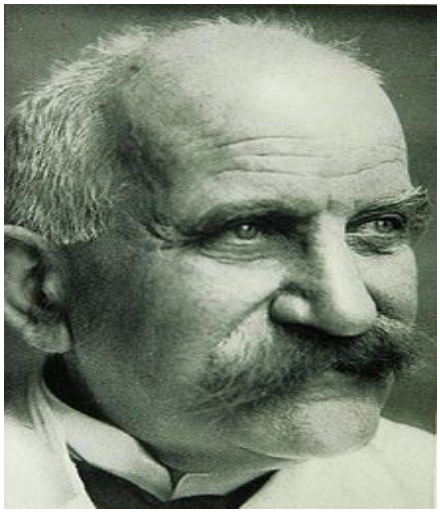
Diagnostic studies for allergic contact dermatitis include the following:

1) **Patch testing**

Pliny the younger noticed people developing itching when cutting pine tress in 1st century AD. Since then, patch testing and contact dermatitis go hand in hand. 17,18,19 centuries- Pre Jaddhasson period researchers reproduced contact dermatitis by applying responsible agents onto intact skin.

In 1884, Neisserdemonstated the same in 8 cases of iodoform dermatitis and described regarding idiosyncrasy and then mercury associated reactions. [16]

Jaddhason in 1895-1896 a who was a professor in Bressaleau university-department of dermatology in Germany had recorded numerous observations in regard to this field.



Joseph (Josef) Jadassohn

September 10, 1863– March 24,1936

Patch test was first employed using blotting paper method 1847 by Staedler. An ophthalmologist named Collin in the year 1889, noted positive outcomes on application of atropine patches to his patients who reported adverse outcomes on using atropine eye drops.[19]

However, Jadassohn has been rightly called the father of patch testing as he first scientifically established the role of patch testing in dermatitis medicamentosa. He recogonised the process of delayed hypersensitivity to simple

chemicals “gray mercury ointment applied on upper extensor arm covered by using a 5cm2 piece of white paper for 24 hours”, and called this patch test.[16]

The most important advance in the field of dermatology clinical practice in the twentieth century was by Sulzberger who highlighted the importance of proper standardization of patch testing to improve the outcome.

Bruno Bloch, Basel 1911 described technique of patch testing. Allergen is placed on a linear stip over the back and covered with a big pieces of guttapercha which is was held in place with zinc oxide adhesive plaster – size of patch – 1cm2. He also graded the skin reactions fom simple erythema to necrosis and ulceration.[16]

In the year 1931, Sulzberger and Wise had made a statement thatin the diagnosis of eczema and allergic contact dermatitis, patch testing should be used which is the single most effective tool in the diagnosis of allergic contact dermatitis.[21]

In 1982 Colman stated that failure to use patch test wherever needed is and abuse.

Fisher in the year 1986 said that a correctly applied and interpreted patch test is a scientific proof of allergic contact dermatitis. He also quoted that patch test is a complete bioassay as compared to the Henle Koch postulates – wherein a microorganism causing the disease must be isolated and should grow in pure

culture and produce the same clinical spectrum when inoculated in a healthy individual.Patch tests also are a purified etiologic agent that reproduces the clinical spectrum in a susceptible host. To achieve this, the following principles have to be used:

1. The test should be performed with a known substance in a standard concentration
2. The test must not be performed when the disease is acute
3. The patient should be given proper instructions as to – leave the patch untouched for 48 hours unless if it burns severely wherein he can remove that alone care fully without disturbing others.
4. The patient should also be instructed not to shower, engage in sports or heavy work
5. Patch should be removed and read on the 2nd day – 48 hours and an additional reading at day5-7 (72-120 hours) using the key of North American contact dermatitis Group.
6. Differentiating allergic from irritant seems to be difficult. Allergic reactions itch more intensely than irritant.[7]

Patch testing is considered as the investigation of choice for detection of delayed hypersensitivity and as a gold standard investigation.[19]

Thus epicutaneous test or the patch test is miniature form of allergic contact dermatitis by applying the suspected allergen and occluding an intact skin of patient with suspicion of contact dermatitis. The same principle of contact sensitivity where in the circulating memory T cells play a role in subsequent exposure is employed to produce a favourable outcome to treat the patient using concentrations that do no irritate the skin.[20]

Patch testing using multiple allergens also helps in impoved and accurate diagnosis. One has to keep in mind the exposure of the patient to all the suspected allergens in the patients environment.[49]

Concurrent medication with immunosuppresants should be avoided at the time of patch testing .Steroids can be used but not more than 15mg/day. To combat the itching antipruritics and antihistamines maybe used.

Diagnosis by patch testing favours the patient in numerous ways – including

- improvement of quality of life
- cost effective investigation
- cost of therapy is less.[21]

Patch testing is done usually by the allergen panels available commercially – most commonly chemotechnique is used. These allergens are loaded in presterilisedfinn chamber (aluminium) with control – usually petrolatum. Secured with adhesive skin tapes.

Removed at 48 hours in broad daylight and read after half an hour which best detects the delayed response and an usual second reading is taken at 72 hours. Some substances although may require a late reading as described by Mark D.P Davis who observed that a delayed positive reaction was noted with palladium chloride,gold sodium thiosulfate, neomycin sulfate, dodecyl gallate, para-phenylenediamine and for corticosteroids.[20]

Apart from this the patch test results are also influenced by the physico-chemical properties – molecular and crystal size, lipophilicity of the molecule.[19]

We shall discuss later in regard to the patch testing in case of corticosteroids later.

Interpretartion of patch test results

It is based on the ICDRG scale –Group ofInternational Contact Dermatitis Research The intensity of the reaction is scored and recorded on the days of patch test reading accordingly. Its crucial for a treating doctor to interpret the outcome. For example, irritant properties of cobalt chloride results in petechial response.

Which can easily mistaken for contact hypersensitivity

For corticosteroids there is an edge effect due to dilution of allergen at the periphery and anti-inflammatory effect of the steroid in centre.[21]

Table – 2
ICDRG SCALE

SYMBOL	PRESENTATION	INTERPRETATION
-	Nil reaction	Negative
?	Erythema No infiltration	Doubtful reaction
+	Apart from erythema, there is infiltration, discrete papules	Weak positive
++	Apart from erythema, there is infiltration, discrete papules and few vesicles	Strong positive
+++	Apart from erythema, there is infiltration, discrete papules and confluent vesicles	Extreme positive
Ir	Vesiculation, blitering and necrosis	Irritant reaction
Nt		Not tested

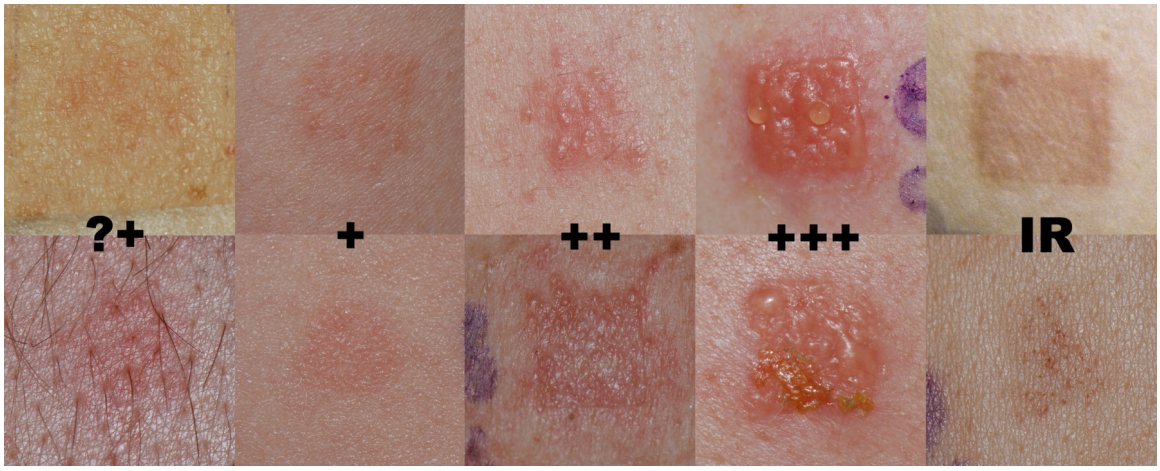


Figure – 2
ICDRG SCALE

2) Repeat open application test (ROAT)

It is particularly useful in patients who have a weak or mild (1+) type of reactions to a particular substance. It thus determines that the reaction is significant or not.[74]

ROAT is most useful when an individual has a 1+ reaction to a chemical found in a leave-on consumer product.

If a patient is 1+ allergic to a topical emollient, the patient is asked to apply the same twice a day behind the ear or neck and observed for reaction. If there is a positive response then the 1+ reaction is considered positive. If there is a negative response then the 1+ reaction can be discounted.[21]

3) Dimethylgloxime Test

It is a chemical analysis wherein the material is tested if it contains a suspected allergen or not. It has been employed in patients suspected to have various allergies including- cobalt chloride, chromium, nickel, formaldehyde etc., This test is used to detect nickel in metallic objects such as watch straps which would thus result in allergic contact dermatitis in sensitized patients.[21]

4) Intradermal testing

Intradermal testing is also used for the detection of allergic reactions to corticosteroids. This method may be of use in situations where inadequate percutaneous penetration of corticosteroids in patch testing may lead to false-negative results.[75,76]

Not all formulations are available for intradermal testing.

Intradermal testing is carried out by an intracutaneous injection of the test formulation with a 0.5 to 1.0 ml tuberculin syringe and 26- or 27-guage needle.

A volume of 0.1ml is injected into the superficial dermis of the flexor aspect of the forearm and a superficial bleb of 2 to 3 mm diameter should be obtained.

A 0.1ml intradermal injection of normal saline should be used as a control. Results should be read at 15 minutes, day 2, and day 4. A 5 to 10 mm wheal is considered to be a positive result. [21]

5) Skin Biopsy

Skin biopsy is rarely indicated in case of allergic contact dermatitis.

It is considered in difficult to diagnose conditions wherein the clinical picture mimics that of psoriasis, lymphoma. However it becomes a difficult task when areas involved are palms and soles which is not unusual.

Histo-pathological examination of allergic contact dermatitis will reveal the following:

- Epidermis may show hyperkeratosis, parakeratosis, acanthosisspongiosis and micro- vesicles
- Dermis will have inflammatory infiltrate mainly comprised of lymphocytes and mononuclear cells
- At times the picture may simulate mycosis fungoides which is espcecially well known in chronic actinic dermatitis which is a form of pohotodermatitis

6) KOH Test

KOH test can be done to rule out fungal infections if any which appears to be a close differential in case of allergic contact dermatitis.

With all this background knowledge on allergic contact dermatitis, we are now discussing in detail about contact hypersensitivity to topical corticosteroids.[75]

MANAGEMENT

The mainstay of therapy will be to address the etiologic factor – the causative allergen in case of allergic contact dermatitis.

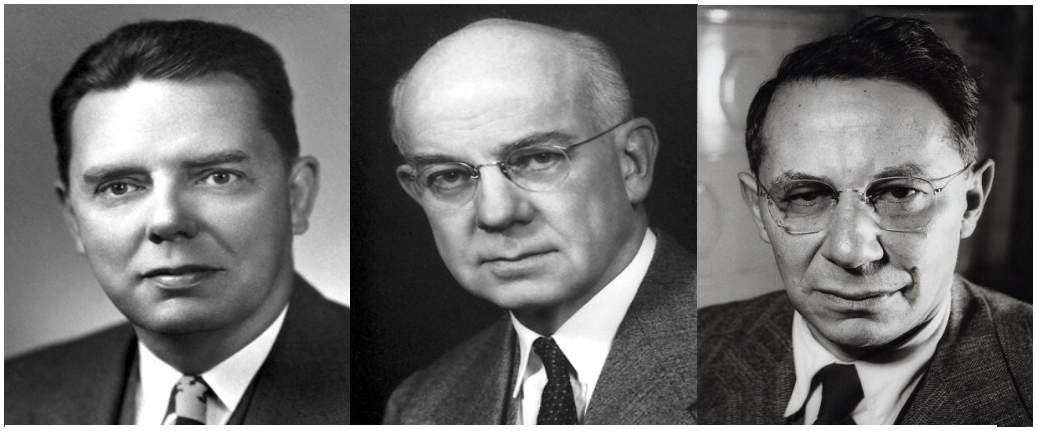
Thus upon identification of the allergen, patient should be informed regarding the same and warned to identify and avoid the same.

They should also be counseled regarding possible cross reacting substances. Emollients are used in almost all patients because of the associated scaling. In acute cases topical corticosteroids or at times wherein there is lots of edema and exudation at widespread areas even oral immunosuppresants may be indicated for a short period of time.[103,104]

Newer modalities of therapy include oral hyposensitisation and reducing the systemic load of the allergen. – commonly employed in nickel allergic contact dermatitis. By employing a diet devoid of nickel or counter act the effect using disulfuram.[15]

TOPICAL CORTICOSTEROIDS

The novel drug in therapy of rheumatoid arthritis using a hormone – cortisone in 1950 fetched a Nobel prize award for Edward Kendall and Philip Hench along with a Switzerland based chemist Reichestein.[1]



Philip Showalter Hench Edward Calvin Kendall Tadeus Reichstein

Topical corticosteroids are the mainstay of treatment of various dermatological disorders including atopic dermatitis, seborrheic dermatitis, contact dermatitis, lichen planus, insect bite reaction, psoriasis, etc., since the introduction of "compound F" or hydrocortisone described in 1950, a natural glucocorticoid that reduces inflammation and proliferations in certain skin disorders.[2]

The mechanism by which it acts areimmunosuppressive, anti-inflammatory, anti-proliferative and vaso-constrictive properties of the corticosteroids. Structural and chemical changes in this lead to the discovery of various strength and properties of corticosteroid molecules. Hence multiple topical corticosteroid creams are available for use.[8]

These effects of corticosteroids are owing to:[24]

- The inhibition of various pro-inflammatory cytokines and transcription factors
- basophils apoptosis
- Expression of the adhesion molcules on the endothelial cells are reduced.
- Inhibition of the capillary dilation, spongiosis, reduction of vascular permeability and lymphocyte function
- Decrease the proliferation of CD8 T lymphocytes[7]

Table - 3

DERMATOLOGICAL INDICATIONS OF TOPICAL CORTICOSTEROIDS[24,25]

GROUP OF DISORDER	DERMATOSIS
Dermatitis	Seborreic dermatitis, Prurigonodularis, lichen simplex chronicus, atopic dermatitis, numular eczema, allergic contact dermatitis.
Papulosquamous	Psoriasis, lichen Planus
Vesicobullous	Vitiligo
Autoimmune	bullous pemphigoid, cictricialpemphigoid, pemphigus foliaceous
Others	lupus erythematosus, dermatomyosistis, morphea, alopecia areata, PUPP, early CTCL, Lichen sclerosis

Table - 4

MECHANISM OF ACTION OF TOPICAL CORTICOSTEROIDS[7,22]

Corticosteroid molecules penetrate though the membrane of the epidermis

A steroid – receptor complex is formed by interaction with the various receptor proteins that are present in the cytoplasmat the cellular level by binds to the glucocorticoid receptor to form a corticosteroid-receptor complex which then translocates into the nucleus

↓

this then binds to the glucocorticoid-responsive element of the target genes which changes the transcription of messenger RNA (mRNA).

↓

This mRNA thus transcribed acts as a template for synthesis of proteins that can have both agonistic or antagonistic effects

Thus stimulating the production of a glycoprotein - lipocortin. Or annexin A1

Annexin A1 is located in the basal keratinocytes cytolplasm of normal skin, whereas in the lesional skin it is translocated at the cell memberane

↓

The release of arachidonic acid from phospholipids by phospholipase A2 which will thus be inhibited by lipocortin

↓

This arachidonic acid is a basis for the formation of leukotrienes.

Corticosteroids also inhibit mRNA responsible for interleukin-1 formation.

↓

These effects on interleukin-1 and arachidonic acid metabolism formation produce reduction in inflammation, immunomodulatory and anti-mitogenic effects.

It also inhibits the transcription of various cytokines involved in atopic or contact dermatitis, such asIFNγ and TNFα

The annexin 1 functions in various levels

This juxtacrine interaction explains the mechanism by which anti-inflammatory process occurs.

It upregulates the glucocorticoid mediated leucocyte inhibition.

Apart from this, there is modulation of mast cells

Antimitotic property – in psoriasis

Apoptosis of eosinophils

Vaso constrictive effects

Immunosupressive is also by suppression of various immune mediators –DC's, macrophages, endothelial cells and fibroblasts[22]

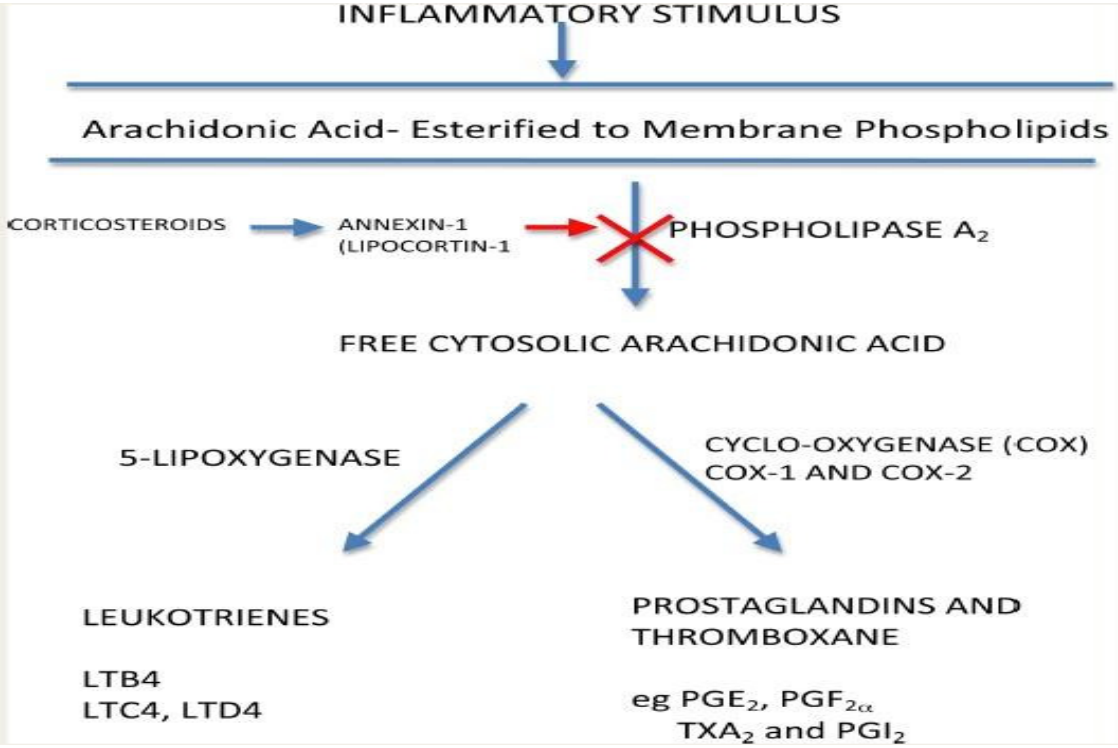


Figure -3 Annexin function

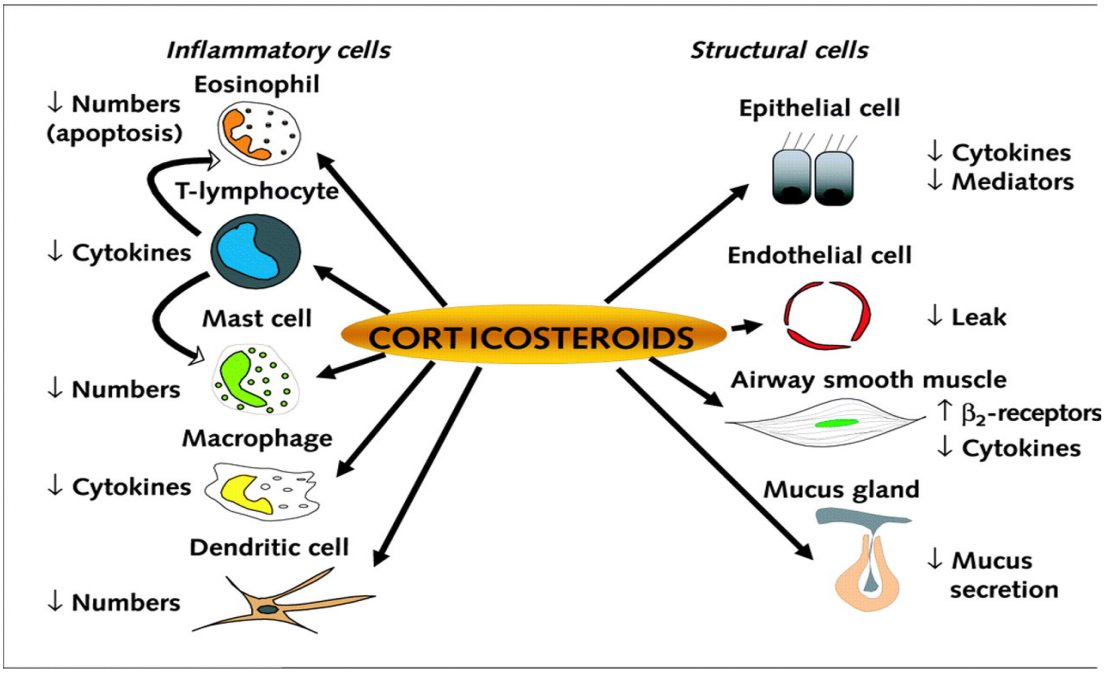


Figure – 4 Corticosteroid Effects

Key factors that should be considered to effectively use the therapeutic properties and decrease the side effects are[25]:

- potency of the active agent
- clinical efficacy of the selected agent,
- vehicle,
- affected site, and
- occlusive used or not.[24]

From hydrocortisone molecular modifications resulted in corticosteroids of varying potency. These include physiochemical alterations byhalogenation or esterification have produced more potent molecules.

Topical corticosteroids depending on their vaso-contrictive properties are classified from mild to high potent. However, it may not always correlate with the therapeutic efficacy.[24]

SITE OF APPLICATION

The diseased site should be kept in mind while deciding upon the use of a particular corticosteroid molecule. As damaged epidermis may result in increased absorption.[27] Soles of the feet or palms of the hand are areas with thick stratum comeum and allow very low penetration. Hence to achieve a good outcome clinically high potent preparations must be preferred.[27]

Parts with thin stratum corneum, such as certain parts ofthe face. Eg.eyelids, scrotum, promote enhanced absorption. Hence are more prone for the adverse effects.

In patients with extensive areas of dermatitis a medium to low potency steroid must be used to minimize the risk of systemic absorption and hence resulting in untoward effects.

POTENCY

Depending on the vaso-constrictive properties classified into I-IV by Stoughton and Cornell in 1985.[22]

Reclassified by British National Formulary. Whereas the American systems classifies the corticosteroids into [7]

Although knowledge of all this is needed each physician should know at least one drug in each class to treat various disorders efficiently with minimal side effects.

Weak steroids are preferred for highly responsive conditions. Eg: flexural psoriasis or atopic dermatitis,

Potent steroids for recalcitrant or less responsive conditions. Eg. palmoplantar or nail psoriasis, lichen planus often require higher potency[22]

Table - 31

CLASSIFICATION BASED ON POTENCY

AMERICAN CLASSIFICATION[2] [3]	BRITISH CLASSIFICATION[23]	REPRESENTATIVE MOLECULES[23]	COMMON INDICATIONS[23]
I Superpotent	I	Clobetasol propionate 0.05% cream/ointment Halobetasol propionate 0.05% cream/ointment Betamethasone dipropionate 0.05% ointment	Alopecia areata Atopic dermatitis Discoid Lupus Hyperkeratotic eczema
II Potent	II Potent	Betamethasone dipropionate 0.05% cream Fluocinolone 0.05% ointment Halocinonide 0.1% cream Mometasonefuroate 0.1%ointment	Lichen planus Lichen sclerosis Lichen simplex chrnoicus Nummular eczema
III Upper mid strength		Betamethasone dipropionate 0.05% lotion Fluticasone propionate 0.005% ointment Triamcinolone acetonide 0.1% ointment Halometasone 0.05% cream	Psoriasis Severe hand eczema
IV Mid strength		Fluocinoloneacetoinide 0.025% ointment Mometasonefuroate 0.1% cream or lotion	Asteatotic eczema Atopic dermatitis
V Lower mid strength	III Moderate	Betamethasone valerate 0.1% cream Fluocinoloneacetonide 0.025% crema Fluticasone propionate 0.05% cream Hydrocortisone butyrate 0.1% cream	Lichen sclerosis (vulva) Nummular eczema Seborrhoiec dermatitis Severe dermatitis Stasis dermatitis
VI Mild		Alcometasonedipropionate 0.05% cream or ointment Desonide 0.05% cream Fluocinoloneacetonide 0.01% cream Triamcinolone acetonide 0.025% cream	Dermatitis of intertrigo, perianal dermatitis
VII Least potent	IV Mild	Hydrocortisone 1% /2.5% cream, lotion, ointment	Dermatitis face Childern[35]

VEHICLE

Vehicle - functions as a carrier for the active drug and also hydrates the skin of the patient hence increasing the penetration of the corticosteroid. While selecting the corticosteroid the area of involvement and pattern of dermatitis.

Corticosteroid formulations available for topical use can be creams, ointments, lotions or sprays.

Ointments-consists usually of petrolatum which thus hydrates the epidermis by acting as a occlusive agent. It is ideal in patients with scaling and lichenification involving thick skin

Creams are cosmetically appealing and less greasy than ointments. It has a larger quantity of petrolatum.

Lotions have water base and hence do not have much of emollient effect. They are non-occlusive and ideal for application on hairy areas and flexures and for weeping lesions.[24]

According to Cornell and Stoughton, vehicle can directly modify the therapeutic as well as the side effects by changing the physicochemical properties of the corticosteroid molecule.

Thus discovery of an ideal vehicle is the potential target of research in this field of dermatology.[22]

OCCLUSIVE DRESSINGS

The permeability of steroid as we discussed earlier is enhanced under occlusion upto 10 fold .[25]

The various occlusive used in clinical practice include wet wraps – guaze or hydrocolloids

Occlusive dressings play a vital role in management of long standing dermatitis like atopic dermatitis which thus helps to minimize the used of long term corticosteroid therapy.

ADVERSE EFFECTS

SYSTEMIC

The factors that facilitate systemic absorption include

- high potent corticosteroid usage
- duration of treatment more than 6 months
- application on diseased skin with impaired barrier
- using occlusive in addition
- applying on large body surface areas

Systemic absorption rarely occurs and if so, results in

Increased blood sugars, Cushings disease, femoral head osteonecrosis , and growth suppression in children

Rarely HPA axis suppression[23]

CHOOSING THE TOPICAL STEROID

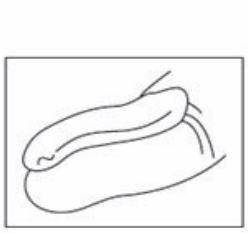
Key factors to be considered include:

1) **Know the disease** : Correct diagnosis of the disease should be made in which there is reasonable evidence of efficacy.

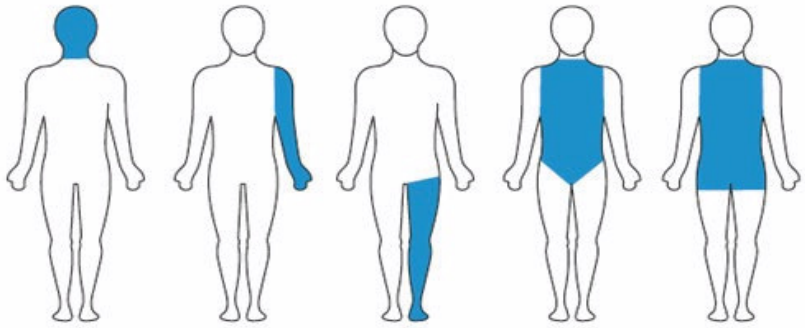
2) **Know the drug**: For selecting the drug- potency, delivery vehicle, frequency of application, duration of application should be kept in mind.

Long and Finlay, described a practical modalitity to measure the amount of topical steroid used for a specific area- termed as finger tip unit.[26]

1FTU is equal to 0.5g or ointment which corresponds to 2 palm surfaces.



One adult fingertip unit (FTU)*



Number of fingertip units (FTUs)

Age	Face & neck	Arm & hand	Leg & foot	Trunk (front)	Trunk (back) inc. buttocks
Adult	2½	4	8	7	7
Children:					
3–6 months	1	1	1½	1	1½
1–2 years	1½	1½	2	2	3
3–5 years	1½	2	3	3	3½
6–10 years	2	2½	4½	3½	5

* One adult fingertip unit (FTU) is the amount of ointment or cream expressed from a tube with a standand 5 mm diameter nozzle, applied from the distal crease to the tip of the index finger.

Figure – 5 Fingertip Unit

Table – 6

SIDE EFFECTS OF TOPICAL CORTICOSTEROIDS

Adverse effects	Clinical presentation	Underlying mechanism
Epidermal	thinning	decrease in epidermal kinetic activity flattening of the dermoepidermal convulsions decrease in the thickness of keratinocyte layer
Dermal	Striae Easy bruisability Blot hemorrhage Melanocyte inhibition	Reduced ground substance and collagen synthesis Risk factors include young age, potency, occlusion, location of application
Combined	Atrophy Telangiectasia Striae Purpura Stellate pseudoscars ulceration	Loss of intercellular substance and dermal atrophy Decreased dermal matrix surrounding the blood vessels
Contact allergy	Allergic or irritant contact dermatitis	More commonly observed in patients with long term dermatitis such as atopic dermatitis, stasis dermatitis, perianal dermatitis
Ocular effects	Exacerbation of herpetic ulcers Increased susceptibility to bacterial and fungal infections glaucoma/ cataract	steroid eye drops andrarely due to potent steroid applications around eyes

Adverse effects	Clinical presentation	Underlying mechanism
vascular effects	rebound phenonmemnon perioral dermatitis rosacea fixed vasodilation	
Hair	hypertrichosis - face & ears lanugo hair alopecia	
Infections	increased incidence of fungal and bacterial infection folliculitis crusted scabies masking of microbial infections -Eg.tinea incognito	
effects owing to pharmacological properties	tachyphylaxis steroid rebound steroid addiction	non compliance excessive vasodilation on withdrawal
Miscellaneous	acneform eruption miliaria urticaria delayed wound healing hypo/hyper pigmentation milia[27]	

SYSTEMIC EFFECTS (rare) include

- HPA axis suppression
- hyperglycemia
- reduced bone mineral density
- edema, hypocalcemia and hypertension

occurs as a result of increased application of high potent steroids increased penetration - Eg. atopic children used under occlusion use in larger areas[27]

SKIN ATROPHY

Commonest and can affect both epidermis and dermis.

Epidermis - changes in epidermis start 3-14 days of treatment, as a result of reduced epidermal size and deceased metabolic activity.

On continual application it can cause thinning of the stratum corneum and absent granular layer. Melanocyte function impairment occurs resulting in hypo pigmentation

Dermis - decreased fibroblast growth, reduced collagen synthesis, resorption of mucopolysaccharide ground substance in dermis, loss of connective tissue support of dermal vasculature.

Influencing factors - Age, body site, potency, occlusion

These changes are reversible but takes months.[27]

Table - 7

VEHICLES USED COMMONLY AND THEIR ADVERSE EFFECTS

ADVERSE EFFECTS	CAUSATIVE COMPONENT
Stinging sensation	lactic acid, urea, formaldehyde, benzoic acid, cinnamic acid compound, sorbic acid
Irritation	Propylene glycol, alcohol, acetone
Urticaria	Formaldehyde, cinnamic acid compound acetic acid, benzoic acid, sorbic acid
Allergic contact dermatitis	Propyl gallate, sorbic acid, parabens, formaldehyde[27]

All these Cutaneous effects are reversible except for atrophic striae which may be permanent.

Rebound effects though rare can occur after abrupt discontinuation of potent topical corticosteroid. The corticosteroids which cause vasoconstriction can cause excessive vasodilatation when it is withdrawn.

Understanding the drug deposition and penetration in the skin will help the clinican in prescribing appropriate duration and frequency of therapy.[93]

Hence optimizing the frequency of application reduces the adverse outcomes including tachyphylaxis and also reduces the expenses which thus improves patient satisfaction.[95]

Moisturisers should be advised daily which can also be used as a sole therapy later. [27]

TACHYPHYLAXIS

It is a phenonmenon observed on long term use of topical steroids.

It's the tolerance a person's skin develops due to the vasoconstrictive effects of topical corticosteroids. After prolonged therapy – the dermal vessels do not constrict well which thus requires higher doses or much frequent application than before.[96]

The ability of these vessels return to normal 4 days after stopping therapy.

Hence a "weekend" or "pulse" therapy resolves this compliance issue or else it can be stopped for 4-7 days and restarted.[23]

MISUSE

Misuse of topical corticosteroids is fairly common in India, as indicated by the proportion of patients visiting dermatologists with adverse effects of these drugs. skin lighteners and along with other irritating skin lightening agents.The adverse effects related misuse include perioral dermatitis, infantile gluteal granuloma, tinea incognito, impetigo incognito and apart from routine.[97-100] It has also noted to delay the diagnosis of leprosyand erythrodermic psoriasis.[28]

ALLERGIC CONTACT DERMATITIS TO TOPICAL CORTICOSTEROIDS

INCIDENCE

The hypersensitivity reactions to steroids are of two types - Immediate reactions[47]: occurring within 1 hour, Delayed - more than half an hour after drug administration. The latter being more common is discussed here.

On reviewing various literature reports the frequency of allergy is 0.2 to 5%. [3,4,13] Prevalence is extremely variable and is influenced by prescribing habits, awareness of topical steroid induced hypersensitivity among doctors, diagnostic procedures. [44-57]

Patients with asthma have a higher incidence than with other conditions[3] of the various risk factors - atopic dermatitis and stasis dermatitis ranks the commonest.[29,108]

CLINICAL FEATURES

Contact allergy to topical corticosteroids needs a high index of suspicion, as clinical presentation is very subtle.[11]Acute weeping eczema is extremely uncommon.[109]

The various presentations include[27]

1. Chronic eczema which gets worse over the yearsinspite of therapy and requirement of large amounts or more potent steroids although avoidance of aggravating factors.
2. Improvement only with specific brands of steroids
3. Requirement of oral steoids or other medications
4. Aggravation of dermatosis on topical corticosteroid application
5. Lack of expected outcome[12]

A common situation is the patient presents with prominent local adverse effects but with persistent complaints.[10]

Browne F. and S.M. Wilkinson suggests that all patients who have long standing or recurrent dermatitis like atopic dermatitis, stasis dermatitis or hand eczemas should at some point be tested for corticosteroid allergy.[30]

DIAGNOSIS

Various methods of detecting corticosteroid hypersensitivity after a clinical suspicion is made includes[8]

1. Patch test
2. Repeated open Application Test[74]
3. Intradermal testing[75]

4. Oral provocation tests[31,78]
5. But before all this a detail history as to [92]
6. Duration of the primary diagnosis for which the topical steroid was used
7. What are the various topical used in the past
8. Duration of application
9. Whether in combination
10. Was it prescribed or obtained over the counter
11. Nature of the medicament – cream, ointment etc., has to be obtained.
12. With all this knowledge we are going to discuss about the most commonly employed investigation in practice

PATCH TEST

Patch testing in a patient with suspected TCS induced allergy needs a in depth knowledge regarding its properties, concentrations that have to be used and the vehicles. Apart from this the controversies underlying the readings, edge effect, false positive and false negative results.[3,32]

A standard series including patients own medicament will be justified. Pitfalls in determinations of appropriate test methods relates to factors such as, the anti-inflammatory effect of corticosteroids, individuals having high sensitizing capacity, bioavailability of the uninvolved patch test site-back / upper arm and not the involved skin which has impaired barrier function.

Usually the concentration of the corticosteroid is low in commericially available preparation, can result in contact hypersensitivity in diseased skin might result in negative outcome on patch testing. Merely increasing concentration of the patch test chemical does not increase its bio-availability.[8]

Allergy due to a topical steroid containing produce can be explained by various factors including

- Excipients (Preservatives, penetration enhancers)
- Allergens in the packaging (Nickel from the tube)
- Active ingredients[27]

False negative reactions in the patch tests can be explained owing to its physicochemical properties:

Molecular and crystal size and lipophilicity.

Lesser concentration of allergen in the skin for hapten protein binding occurs when there is decreased penetration due to lesser solubility of the corticosteroid in the test solution.[31]

Regarding the optimal patch- test preparation, both the vehicle and concentration of allergen is involved. [32]

VEHICLE FOR PATCH TEST:

The optimal vehicle is yet to be determined. There are controversies between two – ethanol and petrolatum.[67-69]

Equivalent patch test results are obtained in case of certain molecules such as tixocortol (Group A) and budesonide (Group B) whereas hydrocortisone 17 butyrate yields better results only with ethanol [33,79]

CONCENTRATION

In patients who are weakly sensitized to TCS molecule, because of its anti-inflammatory effect, it results in a negative response.[70-72]

If its too low – false negatives unless on eczematous site

If its too high - false negatives because of anti-inflammatory effect.

1% dilutions of allergen are more commonly used in various studies for patch testing topical corticosteroids. But Issakson et al suggested that in patients with weak sensitizing potentials lesser concentrations should be used to combat the pharmacological effect of topical corticosteroids as such.[80-91]

For example,0.1% tixocortolpivalate and 0.01% budesonide, 1% for hydrocortisone yields better results.[8]

THE READING

Delayed reading is recommended owing to its anti-inflammatory properties by numerous authors [20,73]

Table – 8

PECULIAR REACTIONS SEEN IN CORTICOSTEROID PATCH TEST

Peculiar reaction	Clinical description	Interpretation
Edge effect	Thin rim of erythema/ papules at the edge at 48 h reading	High inflammatory effect under the chamber
Non-palpable erythema	Faint erythema at 48/96 h reading	Low potency molecules. Becomes positive in day 7 or later
Blanching	Localized pallor at 48 h reading	Highly potent molecules in alcohol due to vasodilation. May become +/- later

EDGE EFFECT

The anti-inflammatory effect that is more pronounced at the site than the edges where the diffusion is present resulting in lower concentration. Thus, results in peripheral erythema or papules around the patch applied site. This is considered positive in case of corticosteroid patch testing.[14]

CROSS REACTIVITY

Dooms Goosens in 1986 observed that patients reacted to tixocortol in patch test where the molecule was not available in the country.[58] This is explained by its structural similarity to the parent molecule – hydrocortisone.[37] This was further confirmed when these patients tested positive to intradermal hydrocortisone injections. Similar cross-reactions were observed with budesonide and triamcinolone.[27]

Before discussing about the cross reactivity patterns certain factors as to how corticosteroids induce allergy and knowledge on the chemical structure is needed.

CORTICOSTEROIDS AS HAPTENS AND POTENTIAL CROSS REACTIVITY

Factors that determine the recognition of corticosteroid molecule includes

- physicochemical structure of the molecule, to which gropu it belongs etc.,

The spatial geometry and the volume occupied by the molecules determine the receptor binding.

True cross reactivity can be explained by the following

Considering A as a sensitizing compound and B as a triggering factor

- A,B are similarphysicochemically
- A is metabolized to forma substance which is identical to B and vice versa
- Both A,B can result in similar substance on metabolisation

co-sensitisation are thus mostly explained by these cross allergic phenomenons.[16] Non fluorinated corticosteroids binds to arginine in the keratinocyte than fluorinated corticosteroids because of rapid metabolic degradation.

PHENONMENON OF CROSS REACTION

The same T-cell receptor can bind to 2 different molecules which are structurally and chemically similar.

Group sensitization – wherein a series of similar molecules often give rise to cross reactions in patients.[16]

The conformation of corticosteroids of the 4 groups analyzed and put forth 2 hypothesis.

1) Corticosteroid molecules are possibly metabolized in similar ways and hence destined to interact with similar type of receptor
2) Esters in C 21 are readily hydrolysed to give the free alcohols whereas esters in C17 are more resistant to hydrolysis due to strong steric hinderence.[34]

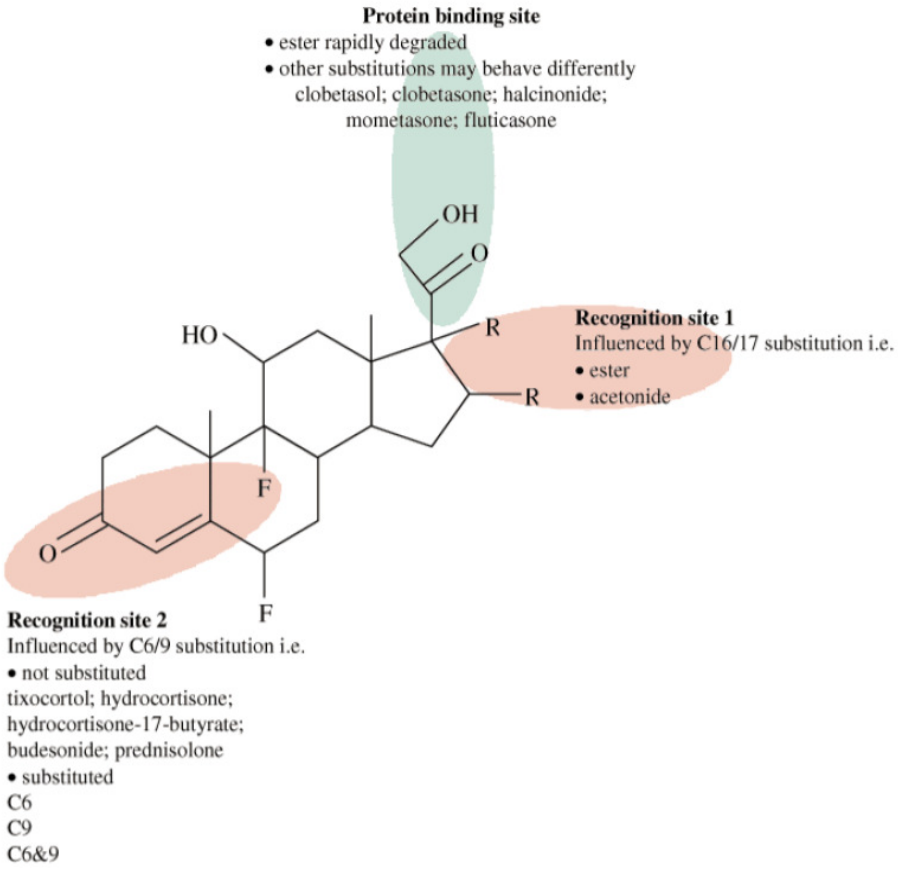
Eg. Tixocortol 21 pivalate – free thiol group in C 21 whereasaclometasonehas in 17,21

All molecules have multiconformational analysis show that the electronic shape that defines the different groups A,B,D and not C.

The volume occupied by specific groups on α face of ring D seems to be critical for the molecular recognition of corticosteroids, while the modifications of the other parts of the molecule seem to have little effect on the recognition patterns.[8]

Figure - 6

SITES IN CORTICOSTEROID MOLECULE THAT DETERMINES CROSS REACTIONS



The allergen is not the steroid on its own but its degradation product[36]

Corticosteroids undergo degradation to reactive glyoxal that then binds with arginine in the keratinocytes to form antigen.

This glyoxal is formed on the C17 side chain on C21 position.

On topical application, the esterase that is present in the epidermis splits any esters present in the molecule resulting in C21 OH group

C21 ester dicarbolic acid- unaffected

C21 ester carbolic acid - > 60% hydrolysed within 30 min (affected)

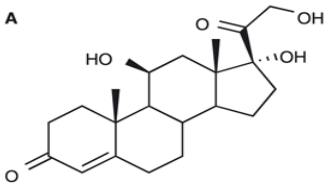
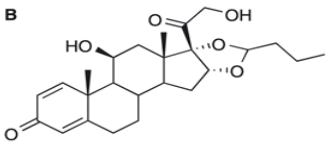
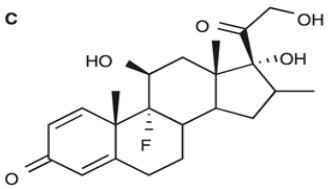
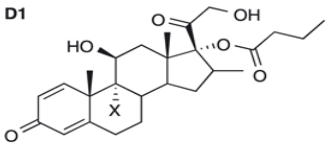
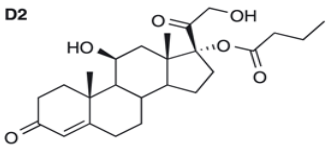
Group	Characteristics of the group	Typical members	Possible cross-reactions
A 	No substitution on the D ring except a short chain ester or a thioester on C_{21}	Cloprednol Cortisone acetate Dichlorisone acetate Fludrocortisone acetate Fluorometholone Fluprednisolone acetate Hydrocortisone Hydrocortisone acetate Hydrocortisone 21-butyrate Hydrocortisone hemisuccinate Isofluprednone acetate Mazipredone Medrysone Methylprednisolone acetate Methylprednisolone hemisuccinate Prednisolone Prednisolone caproate Prednisolone pivalate Prednisolone sodium metasulpho benzoate Prednisolone succinate Prednisone Tixocortol pivalate	D2
B 	C_{16}, C_{17} cis Ketal or diol structure Possibly a side chain on C_{21}	Amcinonide Budesonide Desonide Fluchloronide Flumoxonide Flunisolide Fluocinolone acetonide Fluocinonide Halcinonide Triamcinolone Triamcinolone acetonide Triamcinolone benetonide Triamcinolone diacetate Triamcinolone hexacetonide	
C 	C_{16} methyl substitution on the D ring Halogen substitution No side chain on C_{17} Possibly a side chain on C_{21}	Betamethasone Betamethasone sodium phosphate Desoxymethasone Dexamethasone Dexamethasone acetate Dexamethasone sodium phosphate Diflucortolone valerate Flumethasone pivalate Fluocortin butyl Fluocortolone Fluocortolone caprylate Fluocortolone pivalate Fluprednidene acetate Halomethasone Meprednisone	
D1 	Methyl substitution on C_{16} Halogen substitution Side chain ester on C_{17} Possibly a side chain on C_{21}	Alclomethasone dipropionate Beclomethasone dipropionate Betamethasone dipropionate Betamethasone 17-valerate Clobetasol propionate Clobetasone butyrate Diflorasone diacetate Fluticasone propionate Mometasone furoate	
D2 	No methyl substitution on C_{16} No halogen substitution Side chain ester on C_{17} Possibly a side chain on C_{21}	Difluprednate Hydrocortisone aceponate Hydrocortisone 17-butyrate Methylprednisolone aceponate Prednicarbate	A Budesonide (S isomer)

Figure – 7 Illustration of Group Specific nomenclature

The allergens we used were of the chemotechnique series, which is listed as follows:

Table – 9

LIST OF ALLERGENS USED

ALLERGEN	CONC.%
Budesonide	0.01
Betamethasone-17-valerate	1
Triamcinolone acetonide	1
Aclolometasone-17,21-dipropionate	1
Tixocortol-21-pivalate	0.1
Clobetasole 17 propionate	1
Dexamethazone-21-phosphate disodium	1
Hydrocortisone-17-butyrate	1

C16/17 substitutions influence cross reactivity. [39]

Different isomeric forms of budesonide have shown to resemble both the acetonide structure as well as C17 esters – this explains as to why budesonide is a good patch test screen.[63-65]

90% of individuals who react to budesonide cross react to multiple antigens. [40]

50% of individuals who react to tixocortol cross react.[38,43]

Thus multiple immune recognition sites determine whether a substance cross-reacts or not.[61,64] But this does not happen always, and hence not a rule.[36]

Table – 10

COMMONLY USED TOPICAL PREPARATIONS BY DERMATOLOGISTS IN OUR INSTITUTION

Brand name	Generic name	Group (coopman)
Lobate Tenovate	Clobetasol propionate 0.05%	D1
Betagel	Betamethasone dipropionate 0.05%	D1
Halovate	Halobetasol propionate 0.05%	D1
Momate Elocon	Mometasonefuorate 0.1%	D1
Betnovate	Betamethasone valerate 0.1%	D1
Diprovate	Betamethasone dipropionate	D1
Flutivate	Fluticasone propionate	D1
Dexamet Sofradex	Dexamethasone	C
Desowen	Desonide 0.05%	B
Flucort	Fluocinoloneacetonide	B
Tess	Triamcinolone acetonide	B
Lycor	Hydrocortisone cream0.5% and 1%	A

Apart from these, numerous combination creams are available including double, triple and quadruple type of formulations. [41]Listing of which is tedious.

Those include combinations of salicylic acid and steroids, antibiotic and steroids, antifungals and steroids, all three of them etc., Triple combinations with hydroquinone and retinoic acid are a main stay of therapy in melisma.

Ophthalmic, intranasal, inhalational, intralesional[9] and other preparations for steroids and parenteral [4,60]formulations should also be taken into account as these are reported to cause sensitization. Oral intake of hydrocortisone and methylprednisolone in topically sensitized patients resulting in delayed systemic reactions are rarely noted.[94,59]

Apart from these entire groups where there is labeling, off label uses are there which are commonly misused which includes shampoos, cosmetics etc.,
Apart from this components of topicals steroid formulations which are documented in the past to cause ACD include

- Steroid molecule (active ingredient)
- Propylene glycol
- Parabens
- Benzyl alcohol
- Benzalkonium chloride

Thus delineating that it is crucial to patch test with individual components when the corticosteroid panel is negative.[3,12]

MATERIALS AND METHODS

STUDY DESIGN

Open label prospective observational study

STUDY PERIOD

This observation was held during a period of 1 year in patients suspected to have corticosteroid contact hypersensitivity clinically after obtaining clearance from the ethical committee.

STUDY POPULATION

All patients attending our dermatology out- patient department- males/females, with history of topical steroid application, who do not respond to /or aggravate with topical corticosteroids.

Inclusion Criteria

24 patients aged 14-83 with suspected corticosteroid allergy with history of application of topical steroids were included in this study

Exclusion Criteria

- Patients on systemic or oral steroids(>20mg/day) immunosupressants
- Pregnant and lactating mothers
- Patients with skin lesions on the patch test sites – back and/or arm

SAMPLING METHODS

- Patients were included after obtaining written informed consent
- Patch tests were done on the upper back or arm whichever applicable using Finn chambers with the corticosteroid series+/- ISS provided by the Chemotechnique diagnostics (AB Sweden).
- Patch left in place with micro pore tapes for atleast48 hours and advised not to involve in vigorous activities or allow it to come in contact with water.
- Grading is according to (ICDRG) scale Day 3 (D3), Day 5(D5) and Day 7(D7)
- In addition to this, whenever possible the patient's own medications will be applied –whenever possible the individual allergens were tested if patient had used combination creams.

Table -11

CORTICOSTEROID SERIES

S.No.	ANTIGEN	%
01	Control	
02	Budesonide	0.01
03	Betamethasone-17-valerate	1
04	Triamcinolone acetonide	1
05	Tixocortol-21-pivalate	0.1
06	Aclolometasone-17,21-dipropionate	1
07	Clobetasole 17 propionate	1
08	Dexamethazone-21-phosphate disodium salt	1
09	Hydrocortisone-17-butyrate	1

PATIENTS OWN TOPICAL MEDICATIONS:

DATA ANALYSIS /OUTCOME EVALUATION

- Data obtained have been recorded and documented in the department file.
- Prevalence and clinical patterns of steroid hypersensitivity was determined
- Pamphlets have been issued to the patients containing the information about the allergen with which he/she has tested positive in patch testing and list of common medicaments containing the allergen. Also, in brief about possible cross allergies and hence importance of informing the treating physician/ dermatologists
- Hence we could thus educate the patient on prevention of exposure to the allergen.

RESULTS

Table - 12

AGE SEX DISTRIBUTION

Age in years	Sex		Total	Percentage %
	Male	Female		
10 - 20	1	0	1	4
21 - 30	1	2	3	12.5
31 - 40	5	2	7	29
41 - 50	1	1	2	8.3
51 - 60	2	0	2	8.3
61 - 70	4	0	4	16.9
71 - 80	3	0	3	12.5
81 - 90	0	2	2	8.3
Total	17	7	24	

Inference: males > females ; commonest age 31-40

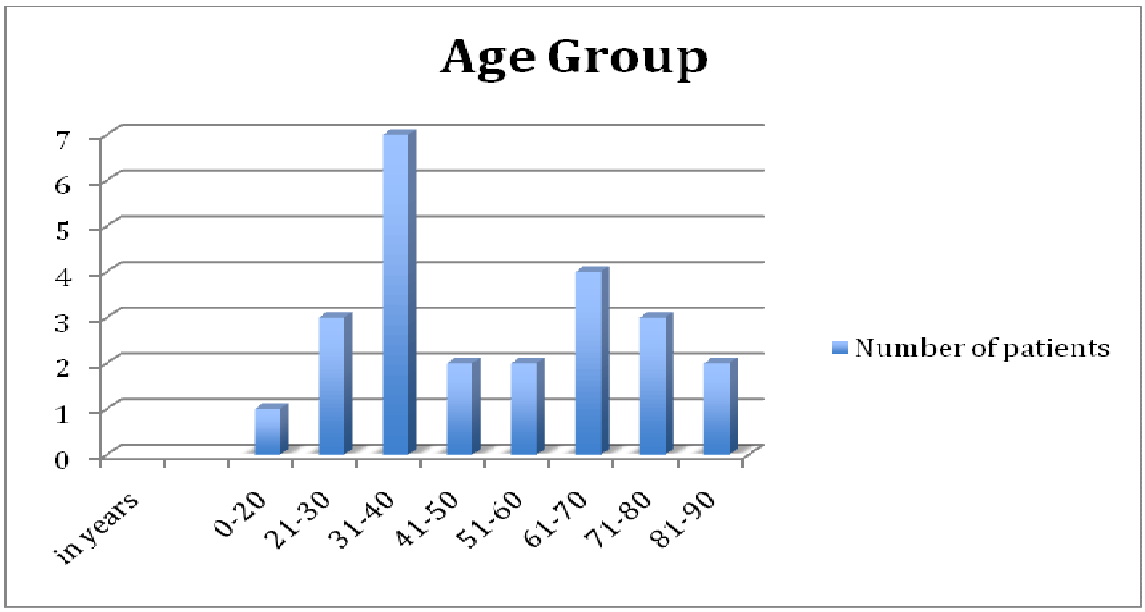


Figure – 8 Age Group

Male: Female Ratio

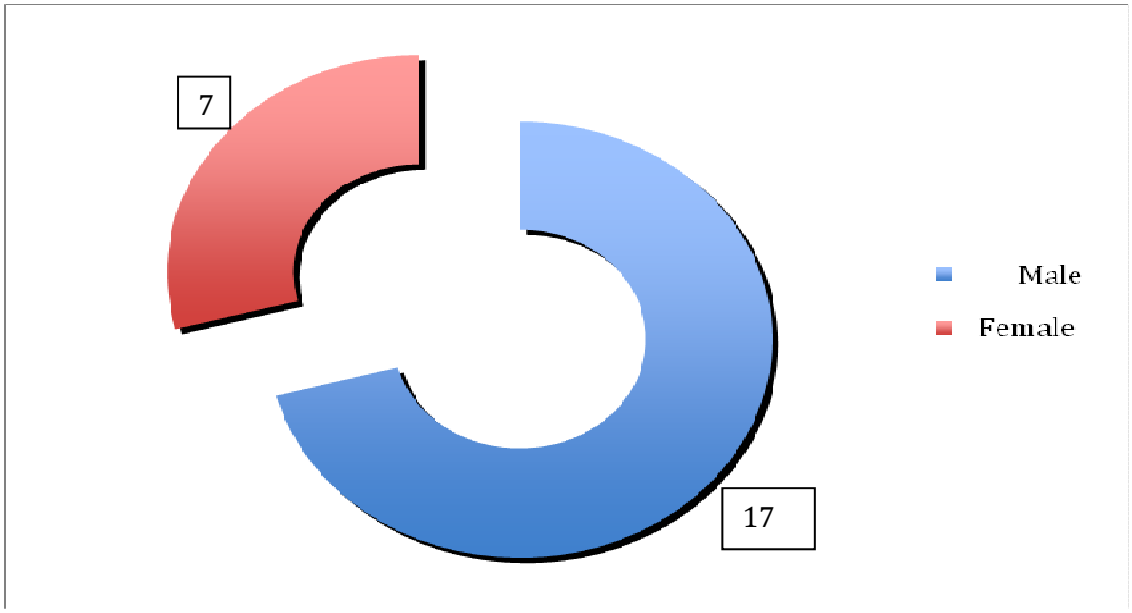


Figure – 9 – Male Female Ratio

Males – 70.8%, Females 29.2 %

Table - 13

DURATION OF COMPLAINTS FOR WHICH TOPICAL STEROID WAS APPLIED

Duration of complaints in months	No. of patients	%	No.of patients with positive patch test	%
0 - 6	6	25	0	82.4
6 - 12	2	8.3	0	58.3
12 - 24	6	25	0	71.4
24 - 36	5	21	0	62.5
36 - 65	3	12.5	3	83.3
65 - 72	2	8.3	1	

Inference: Possible correlation of duration of the complaints directly proportional to the patch test positivity.

Patch test positivities are noted in duration more than 3 years.

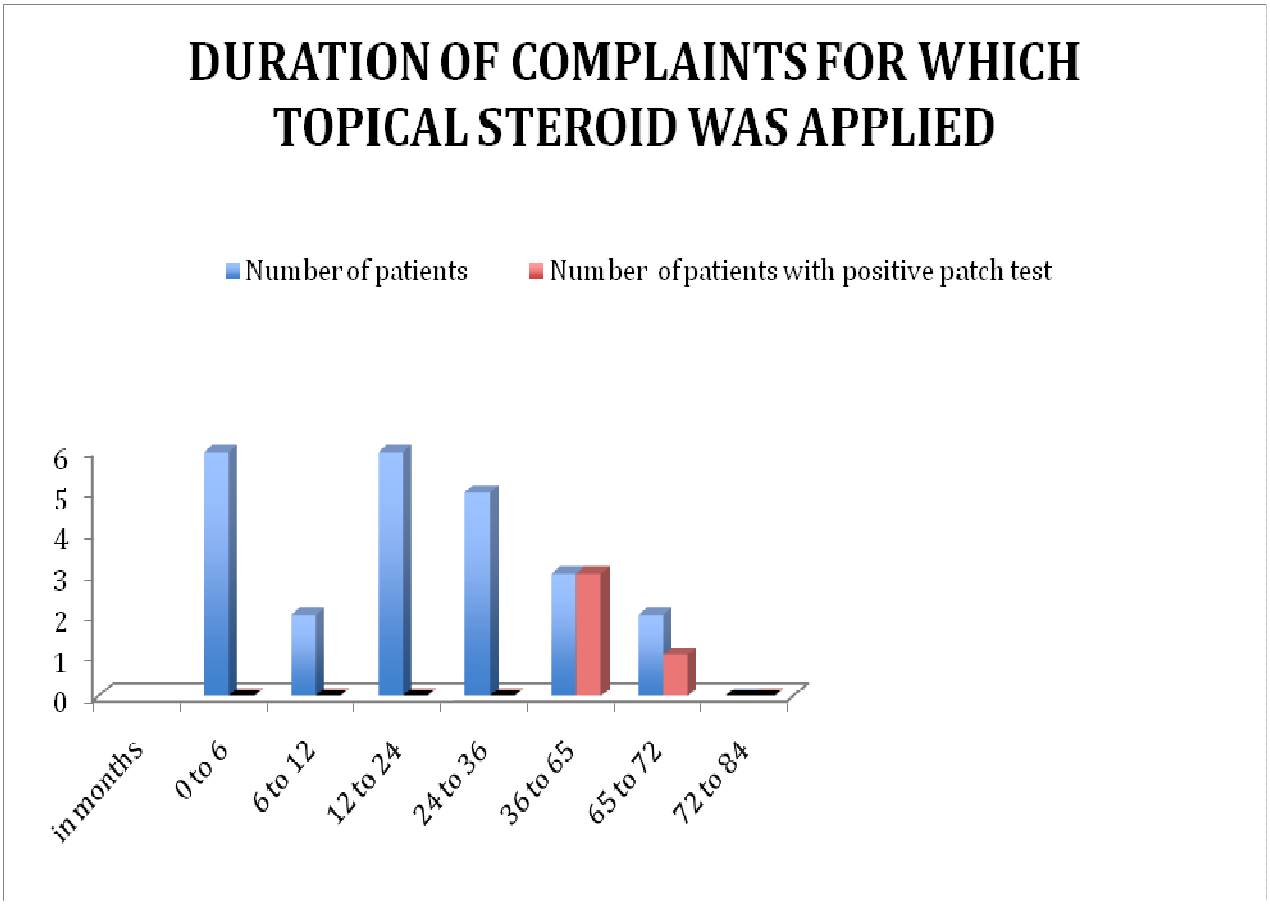

DURATION OF COMPLAINTS FOR WHICH TOPICAL STEROID WAS APPLIED
Number of patients
Number of patients with positive patch test
6
5
4
3
2
1
0
in months
0 to 6
6 to 12
12 to 24
24 to 36
36 to 65
65 to 72
72 to 84

Figure – 10

Table - 14

PRIMARY DIAGNOSIS

S.NO	Primary diagnosis	Number of patients	Percentage %
1.	Palmoplantarpustulosis	2	8.3
2.	Bullous pemphigoid	1	4
3.	Lichen simplex chronicus	1	4
4.	Perianal pruritis	2	8.3
5.	Atopic dermatitis	7	29.6
6.	Seborrheic dermatitis	1	4
7.	Allergic contact dermatitis	4	16.9
8	Psoriasis	1	4
9	Stasis dermatitis	4	16.9
10	Hailey Hailey disease	1	4

Inference: most common among atopic followed by stasis and allergic contact dermatitis

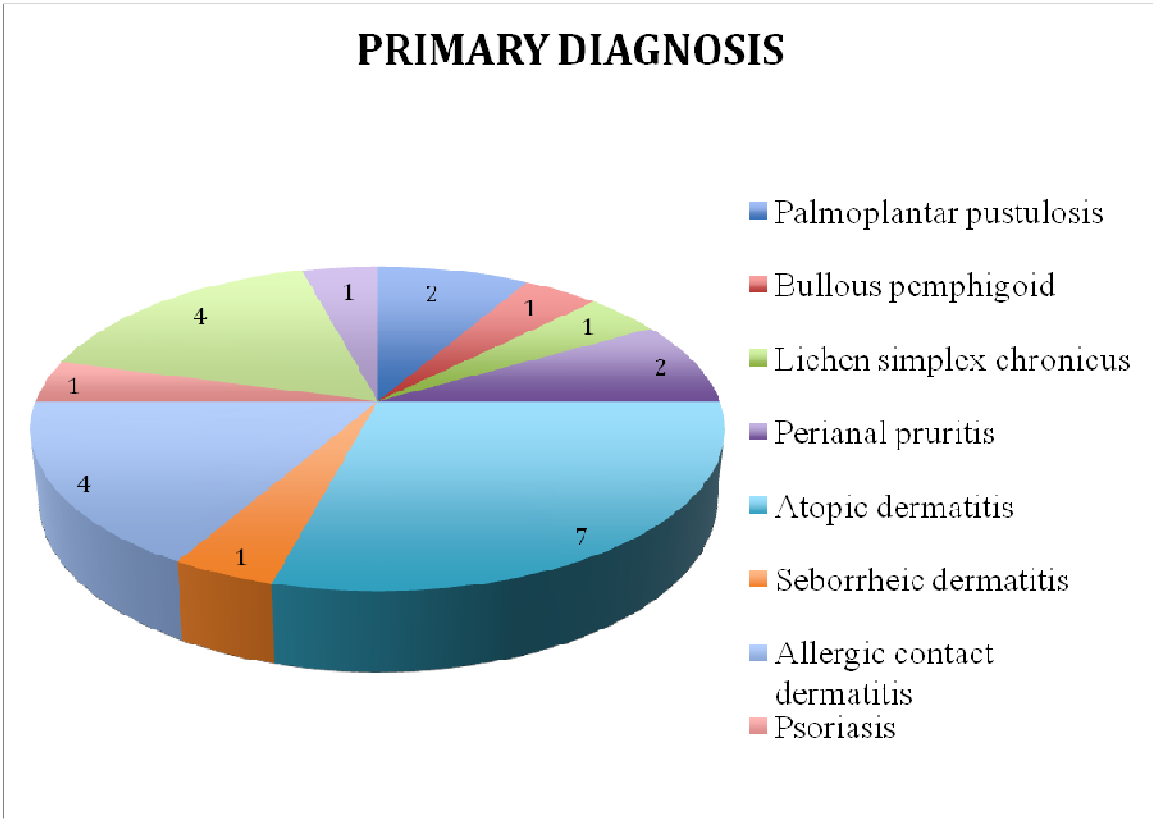


Figure – 11

1-7 Indicates the number of patients with the particular diagnosis

Table - 15

PAST TREATMENT DETAILS

S.No	Topical preparations	Number of patients Applied	Percentage
1.	Emollient	23	95.8
2.	Antibiotics	10	42
3.	Steroid	24	100
4.	Combination	7	29

Inference: All patients were on on steroid molecule or other.
All were on emollients except a case of bullous pemphigoid

7 patients were on antibiotic steroid combination

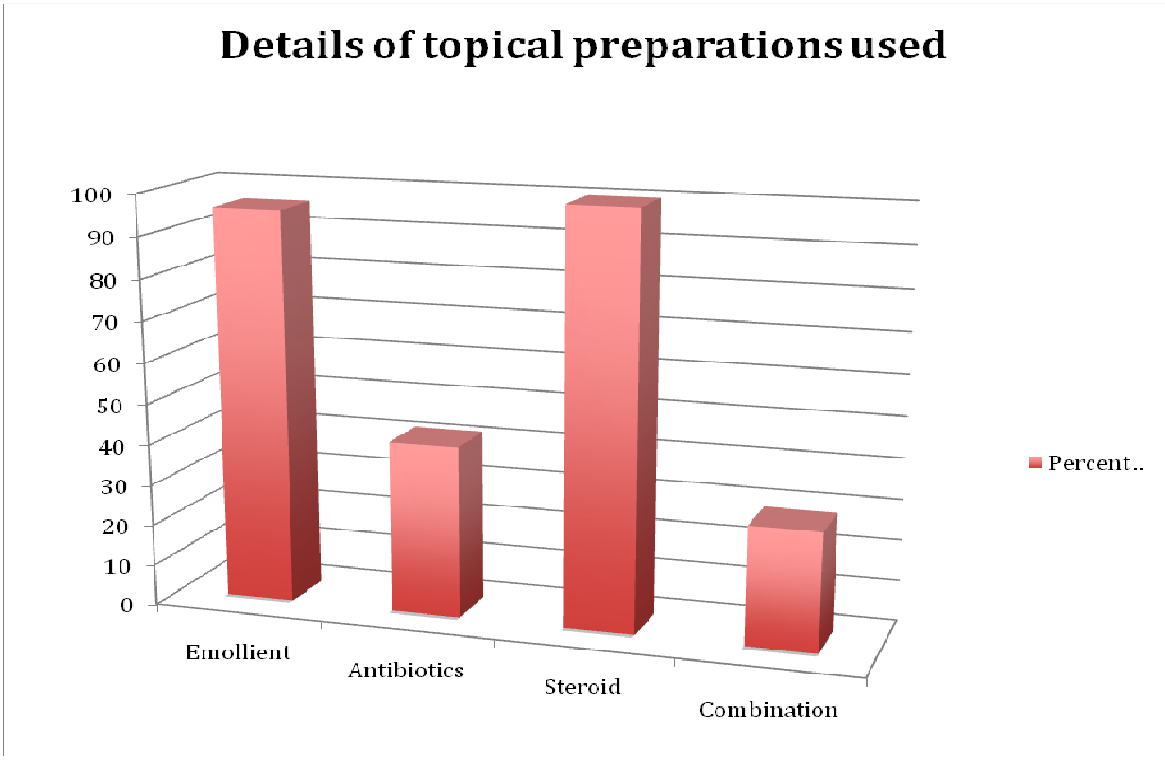


Figure - 12

Table - 16

DETAILS OF TOPICALS

S.No	Steroid brand name(generic name		Antibiotic combinations
1	Diprovate Flutivate	(Betamethasone dipropionate) (Fluticasone propionate)	-
2	Propysalic NF Flucort H	(Clobetasol propionate 0.05%) (Fluocinoloneacetonide)	T-Bact (mupirocin)
3	Momate XL Dipgenta	(Mometasonefuorate 0.1%) (Clobetasol propionate 0.05%)	T-Bact (mupirocin)
4	CFT-CP -	(Fluocinoloneacetonide)	CFT-CP ciprofloxacin, clotrimazole, neomycin
5	Tenovate	(Clobtasol propionate 0.05%)	
6	Betagel	(Betamethasone diprop 0.05%)	
7	Momate	(Mometasonefuorate 0.1%)	
8	Halovate F	(Halobetasol propionate 0.05%)	Haolvate F- fusidic acid
9	Tenovate	(Clobetasol propionate 0.05%)	
10	Halovate Psoricort Dexomet Momate Betnovate GM	(Halobetasol propionate 0.05%) (Clobetasol propionate 0.05%) (Dexamethasone) (Mometasonefuorate 0.1%) (Betamethasone valerate 0.1%)	Betadine Betnovate GM - gentamycin

11	Flutivate	(Fluticasone propionate)	Betadine T- Bact (mupirocin)
12	Sebowash -	(Fluocinoloneacetonide)	
13	Tenovate	(Clobetasol propionate 0.05%)	
14	Tenovate	(Clobetasol propionate 0.05%)	
15	Betnovate	(Betamethasone valerate 0.1%)	
16	Flutivate	(Fluticasone propionate)	
17	Halobaetasol	(Halobetasol propionate 0.05%)	T- Bact (mupirocin)
18	Momate	(Mometasonefuorate 0.1%)	
19	Fucibet	(Betamethasone valerate 0.1%)	
20	Betnovate GM	(Betamethasone valerate 0.1%)	Betnovate GM (Gentamycin)
21	Topinate	(Clobetsol propionate 0.05%)	
22	Betagel G	(Betamethasone dipropion0.05%)	Betagel G (Gentamycin)
23	Flutivate Elocon Desowen	(Fluticasone propionate) (Mometasonefuorate 0.1%) (Desonide 0.05%)	
24	Tenovate	(Clobetasol propionate 0.05%)	

Table – 17

PRESENTING COMPLAINTS

S.NO	Presenting Complaints	Number of patients	Percentage%
1.	Poor / Failure of response	20	83.3
2.	Worsening	4	16.7

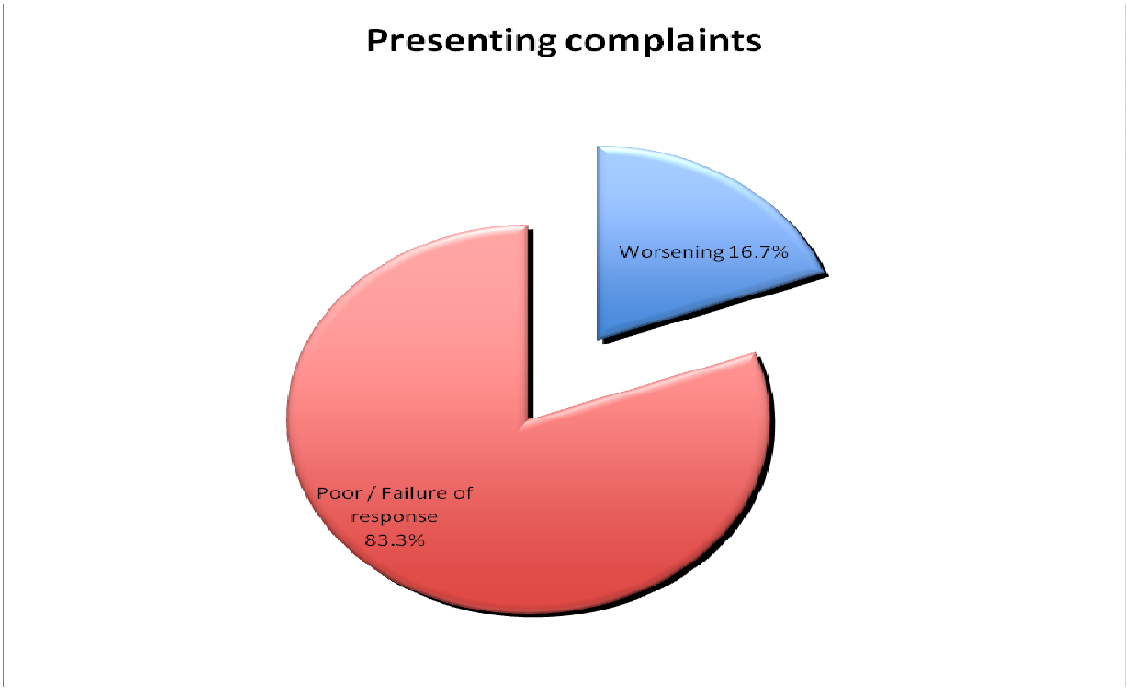


Figure -13

Table - 18

FREQUENCY OF ALLERGEN POSITIVITY IN THE CORTICOSTEROID SERIES

S.No.	Allergen	No. Of Patients	Percentage
1	control	0	0
2	Budesonide 0.01%	0	0
3	Betamethasone 17 valerate 1%	0	0
4	Triamcinolone acetonide 1%	1	4
5	Tixocortol-21-pivalate 0.1%	2	8.3
6	Alclomethasone 17,21 dipropionate 1%	0	0
7	Clobetasol 17 propionate 1%	0	0
8	Dexamethasone-21-phosphate disodium 1%	1	4
9	Hydrocortisone-17-butyrate 1%	0	0
	Total	4	16.3

Inference: Of the 24 patients, 4 patients tested positive (16.3%).
Tixocortol is the most common allergen in this study which was found to be positive in 2(8.3%) followed by Dexamethasone in 1(4%) Triamcinolone in 1(4%)

Apart from this of the allergens tested using Patient's own products - flutivate and desowen was positive in 1(4%) patient.

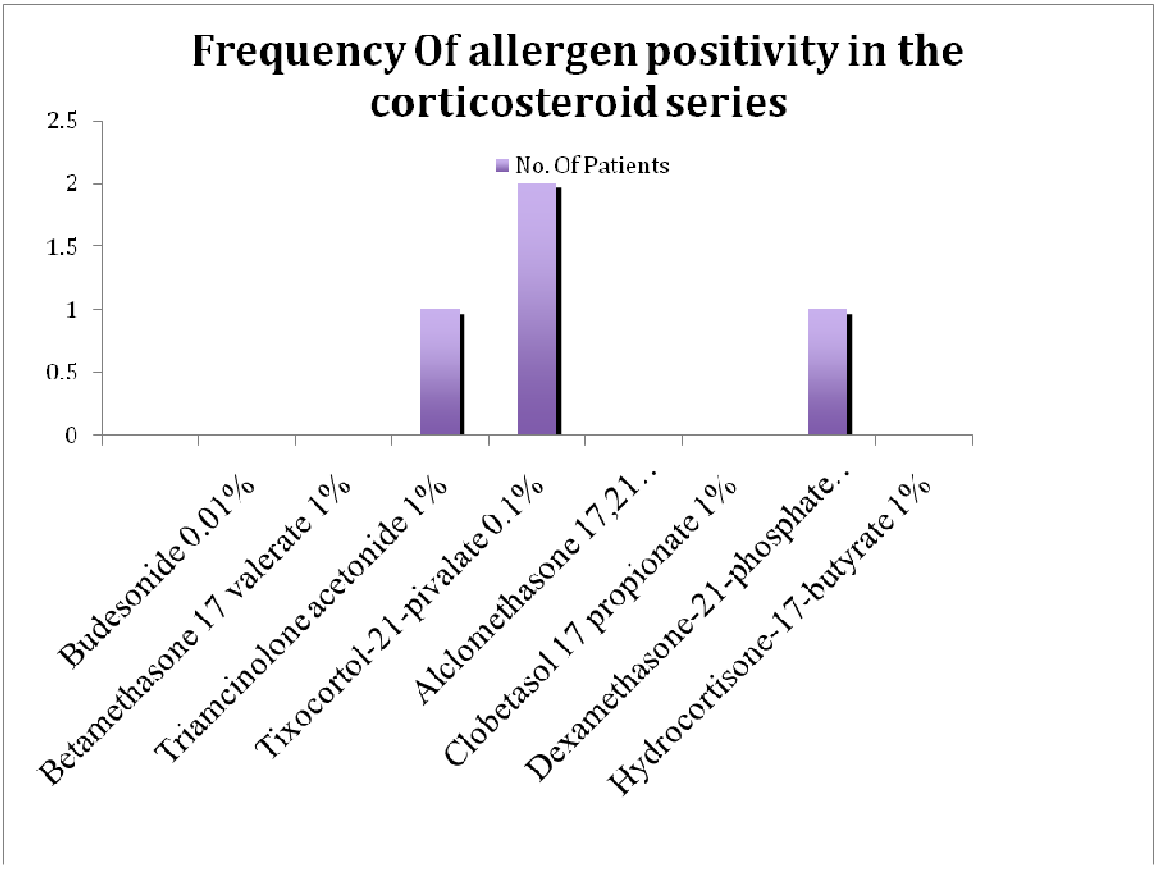
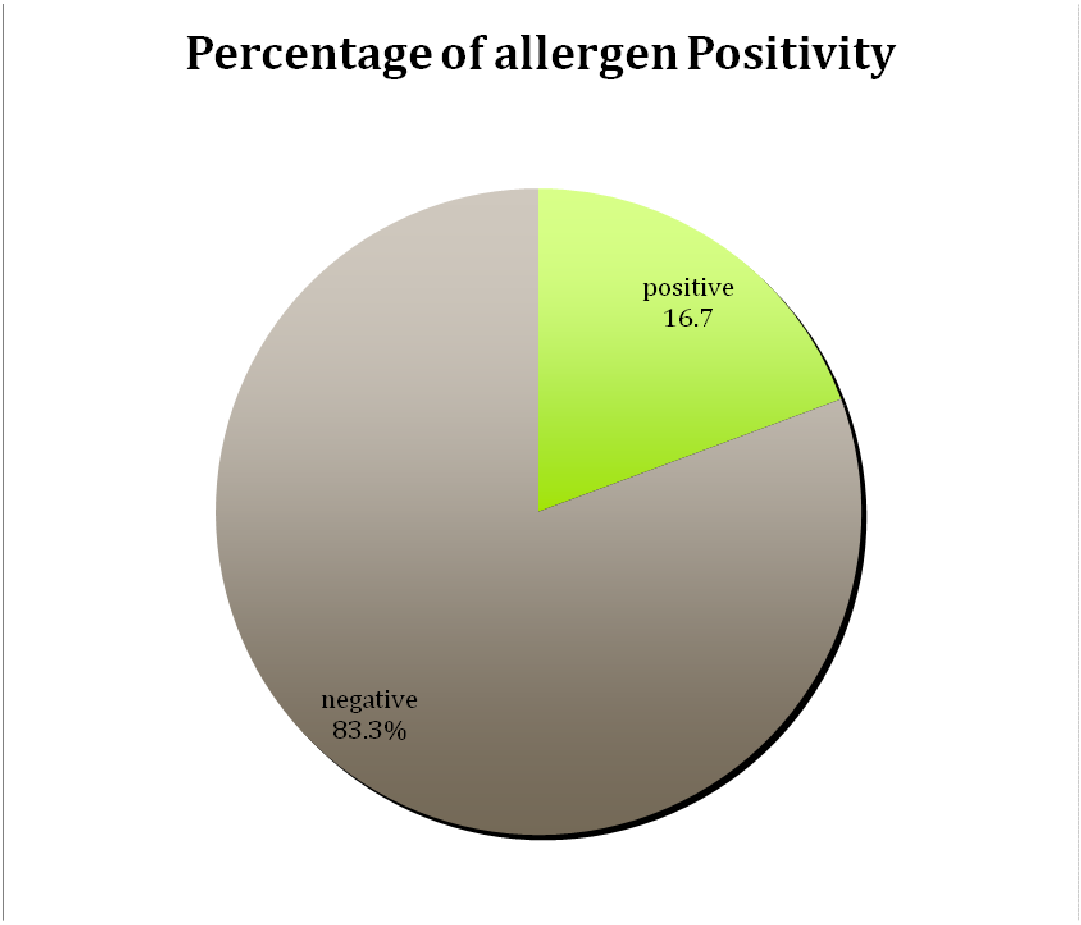

Frequency Of allergen positivity in the corticosteroid series
No. Of Patients
2.5
2
1.5
1
0.5
0
Budesonide 0.01%
Betamethasone 17 valerate 1%
Triamcinolone acetonide 1%
Tixocortol-21-pivalate 0.1%
Alclomethasone 17,21..
Clobetasol 17 propionate 1%
Dexamethasone-21-phosphate..
Hydrocortisone-17-butyrate 1%

Figure - 14


Percentage of allergen Positivity
positive
16.7
negative
83.3%

DISCUSSION

Topical corticosteroids constitute the main armamentarium in the treatment of various dermatological indications. [32] This most useful anti-inflammatory drug has been studied extensively in the recent past in respect to its hypersentivity reactions.[12]

Inspite of the fact that corticosteroids decrease the Langerhans cell population and thus their immune functions, it cannot prevent its hypersensitivity. Type IV (delayed) hypersentivity is more common than Type I hypersensitivity react ions.[11]

The corticosteroids are compounds with low molecular weight and are haptens that only on binding to proteins in human body induce a hypersensitivity reaction.[31] In 1980 Bundgaard studied the properties of corticosteroids which get degraded to corticosteroid glyoxal 21- dehydrohydrocortisone, which reacts with skin proteins like guanidyl resulting in ketoaldehydes.

Groups of arginine and results in formation of the antigenic complex. On this background if we look into the carbon substitutions in detail the non fluorinated corticosteroids degrades and reacts with arginine more rapidly than the fluorinated corticosteroids.[36]

The first report of the description of corticosteroid allergy is in 1959. [37]The incidence of these allergic contact dermatitis ranges from 0.2 to 5%.[3] A study by north American contact dermatitis group NACDG reported it to be 3.1% and in England the same was estimated to be 4.9%.[12]

This huge variability relates to easy availability, the frequency and amount of of the topical steroid used, geographic variation, type of steroid used and the different methodologies of patch testing in terms of the panel, vehicle, concentration and reading times.[61-77]

The scenario in Asia is such that only limited data are available in this respect which demands more extensive studies in establishing the patterns of allergy in the asian population. [3]A study in South east Asia revealed a positivity rate of 3.29% amongst all patch tested patients over a 10 year period in Thailand.[110]

Indian scenario is also influenced by the fact that there are numerous double and triple combination creams, including Kligmann's formula in the market over the counter and are available in numerous fairness creams and is used as cosmetic prepararations.[28] Very poor awareness regarding the need for reading labels and importance of information on how to use and duration of application.

There is no data on the exact prevalence of the topical steroid induced contact dermatitis in our country. [28]

The clinical picture varies from modest inflammatory changes to frank dermatitis with exudative lesions being fairly uncommon.[30] The subtle presentations include an dermatosis that is unresponsive to steroids or only improve on specific brands of steroids ; worsening of preexisting dermatosis on application of topical steroids.[12]

The patients who are sensitized to corticosteroids are most often allergic to other substances like preservatives and antibiotics. [8]

Degreaf, Goosens et alobserved that co-sensitisation occurred in 82% of patients with atleast one other allergen. [50]

Of the various diagnostic modalities patch testing is the major method of detecting Type IV hypersensitivity- practical and feasible.[45,77] In patients where corticosteroid hypersensitivity is suspected the standard patch is applied and in addition to the 48 and 72 hours a delayed reading is absolutely necessary without which 30%of the allergic reactions are likely to be missed.[20,73]

This may be explained by the fact that the intrinsic anti-inflammatory action may suppress or delay the cutaneous response. [37]

The pattern of patch test positivity in corticosteroids is influenced by numerous factors as discussed earlier. [66-73]These include:

- test concentrations
- vehicle chosen
- necessity of late readings
- edge effect
- false negative and
- false positive reactions

Considering all these factors, and the classification of corticosteroid by Coopman based on the chemical structure[35,36]

We review our patient results of corticosteroid patch testing which was conducted in 24 patients with suspected corticosteroid allergy and positive outcome obtained in 4 of them (16.7%)

Reviewing the demographic data

The commonest age group of involvement was on the third and fourth decade (31-40 years) and males (29.2%) affected more than females (70.8%).

Longer duration of application of topical steroids was associated with more incidences of corticosteroid patch test positivity. In our study all positivities were in patients who applied topical steroids for more than 3 years. Similar observation was made by Gonul M who noticed ACD to TS was more common in patients who used it 1 years or more. [30]

Of the various causes of patients presenting with complaints that gave rise to suspicions of corticosteroid allergy the most common diagnosis in these patients were Atopic dermatitis followed by stasis dermatitis and allergic contact dermatitis to other substances. Similar results were found in study done by M. Baeck et al[8] and also MuzeyyenGonul et al. [30]This can also be explained by the chronicity of the condition and requirement of long term application of corticosteroids in these patients.

All patients were on multiple topical preparations. Which included emollients and topical steroids and considerable about were combinations. Combinations were either steroids with antibiotics or steroids with antibiotics and antifungals.

In addition to the routine corticosteroid series we also patch test for patients own medications. [12,87]

This resulted in some interesting observations.

For example, in Case No. 23 a female patient who is a case of allergic contact dermatitis to kumkum (Patch test proven) who was on topical steroids on and off for long duration prior to our investigation presented with worsening of lesions on applingflutivate. Now keeping in mind the fact that fluticasone is not present in our coricosteriod panel (chemotechnique) we went ahead with our routine procedure – costicosteroid patch test and patient's own patch test which included fluticasone (Group D1) (as Flutivate ointment, GSK) Desonide (Group B) (as Desowen cream) and mometasone (Group D1) (as Elocon ointment).

She tested positive initially to tixocrtol on day 3 and 5. Flutivate was positive throughout; Desowen disappeared after day 3 Elocon tested negative. Now, on reviewing the literature, there are studies stating that Group A (tixocortol) cross reacts with group B and group D1 (fluticasone) .

But all this said and done, a study by Wilkison and Baeck[44] as quoted by Fisher's have included Group C and mometasone and fluticasone as "hypoallergenic" which is attributed to the following facts. Novel substitution at C17 in mometasone and fluorine at C6 and C9 rather than C17 are thought to be responsible for lesser cross reactivity.[7]

There are other articles also supporting the fact that fluticasone is a rare sensitisor. [101]

In Case No. 16, a male patient who presented with perianal dermatitis who tested positive to triamcinolone which was consistent from Day 3 to Day 7 tested negative to his own preparation (Flutivate). But we should keep in mind that the flutivate was his current preparation and limited data was available as of his previous therapy.

As we discussed earlier there are studies stating cross reactivity between group A, B, D1. Hence that could explain the reaction to triamcinolone (Group B) which is not a commonly used commercial drug on skin.[34]

Apart from this , 2 patients – Case No. 20 and Case No. 12 who had reacted to hydrocortisone and tixocortol respectively on Day 3 had no reactions at the site on Day 5 and Day 7.

Considering this, on our literature review although there are evidences supporting late reading,[12,37] a study by Mark D.P Davis who conducted corticosteroid patch testing in 1188 patients who came across similar problem were they had to exclude the reactions which appeared on intial evaluations as irritant stated that it could thus be possible that few of these reactions which were interpreted as irritant might be a positive reaction. They also observed that in

addition Day 7 readings detected only an additional 2 out of the 135 positive patch patients. Thus concluded that in their experiences extended reading are of limited value. [45]

One should also keep in mind the fact that all these patients react to the commercially available preparations which consists of vehicles which can increase the penetration of the corticosteroid molecule that done in patch test with neutral vehicle. [3]

Apart from this 2 patients also reacted to T- Bact ointment.

But a much detailed evaluation and preservative series patch testing is needed in these cases to determine the exact cause.

Considering all of the above mentioned facts corticosteroid patch testing has numerous pitfalls which are debatable at multiple levels and needs a in depth understanding of the nature of the molecules and the response of the patients. Any lab investigation cannot reproduce the same allergic response is a fact.[76]

All 4 patients who tested positive to corticosteroid molecules were explained regarding the avoidance of allergens and also counseled regarding possible cross reactivity and that to inform every treating doctor the same.

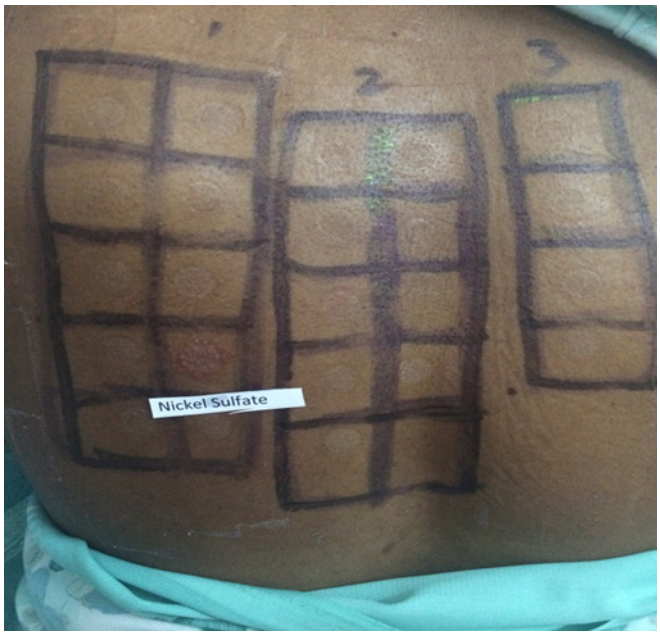
Moreover according to M.Baeck et al, rarely can a dermatologist achieve a prescription which can avoid the corticosteroid allergy because of increased frequency of cross sensitisation.[8]

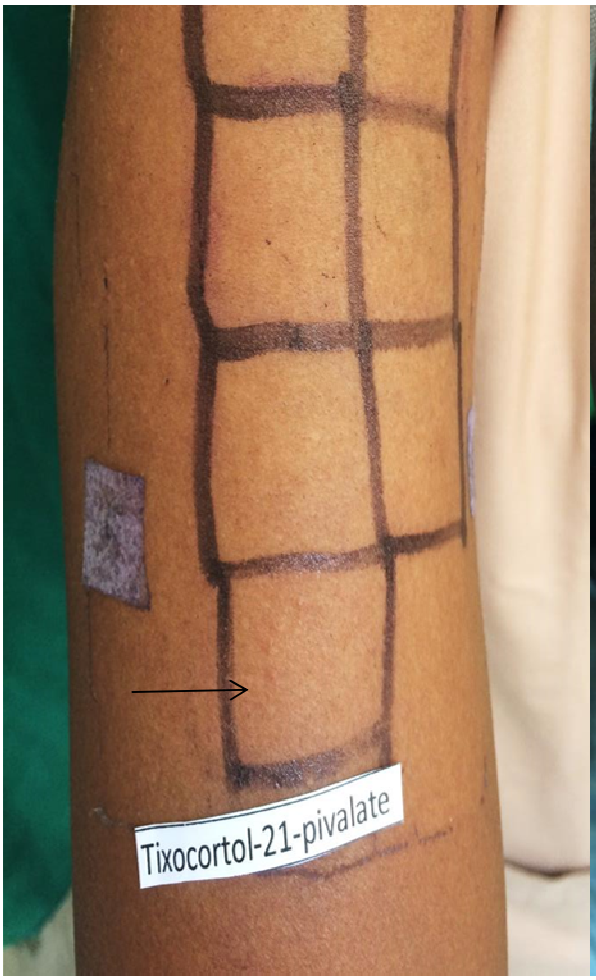
Further studies are still needed in regard to the same.

CONCLUSION

Contact hypersensitivity to corticosteroids is thus a clinical entity that has to be kept in mind by all treating doctors. In our study we detected that 16.7% - 4 out of 24 patients with suspected corticosteroid hypersensitivity tested positive. Hence high index of suspicion and awareness regarding the clinical patterns, cross reactivity and need for diagnosis of contact hypersensitivity to topical corticosteroids is thus mandatory. The patients who are diagnosed to have corticosteroid hypersensitivity in the patch test results should be counseled appropriately so as to achieve a better therapeutic outcome in both systemic as well as local corticosteroid therapy.

39 year old female patient with recurrent scaling and fissuring of hands who was treated with multiple steroids, who initially responded and later had a poor response was patch testing with both ISS and steroid series. ISS revealed nickel sensitivity and steroid series revealed sensitivity to tixocortol 21 pivalate.

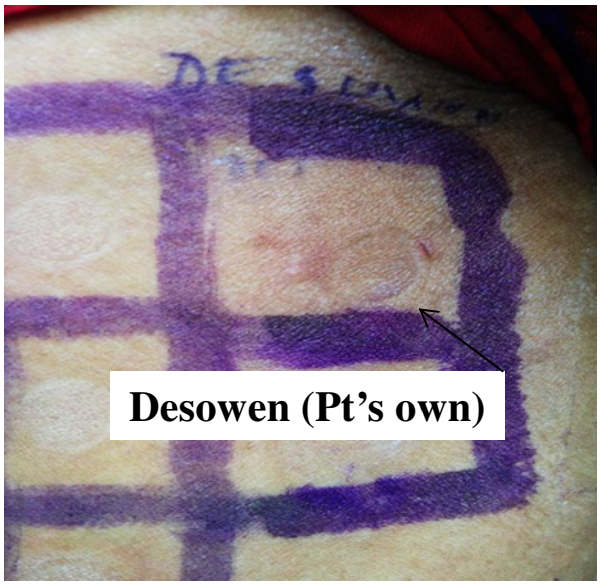




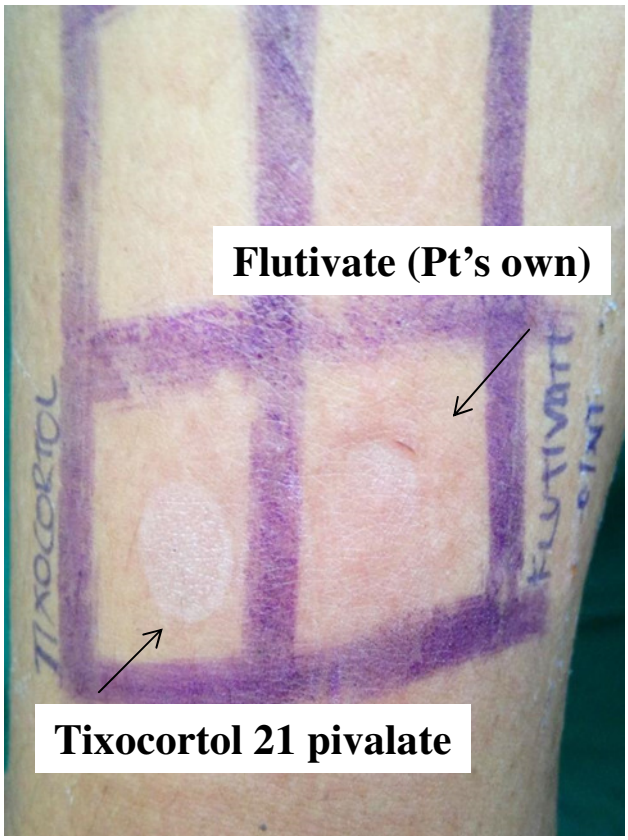
Day 5

Day7

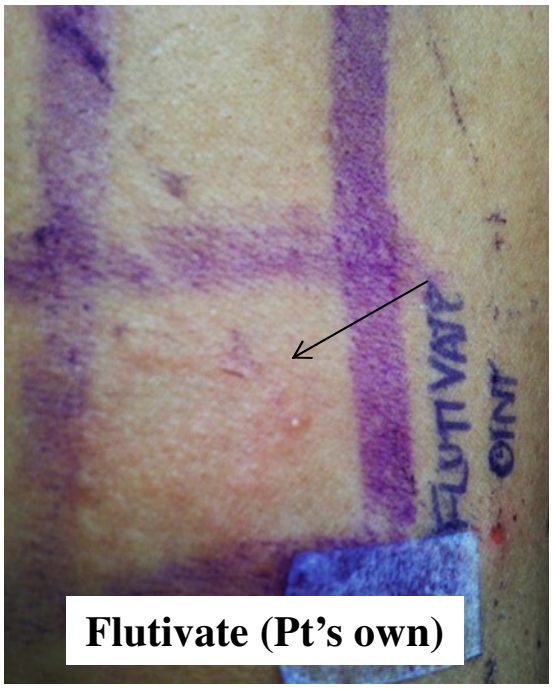
46 year old female patient a case of allergic contact dermatitis to kumkum of long duration who was treated with steroids in past which initially responded and now aggravated – patch test with corticosteroid revealed tixocortol 21 pivalate positivity and on testing with her own medications - flutivate positivity



Day 3

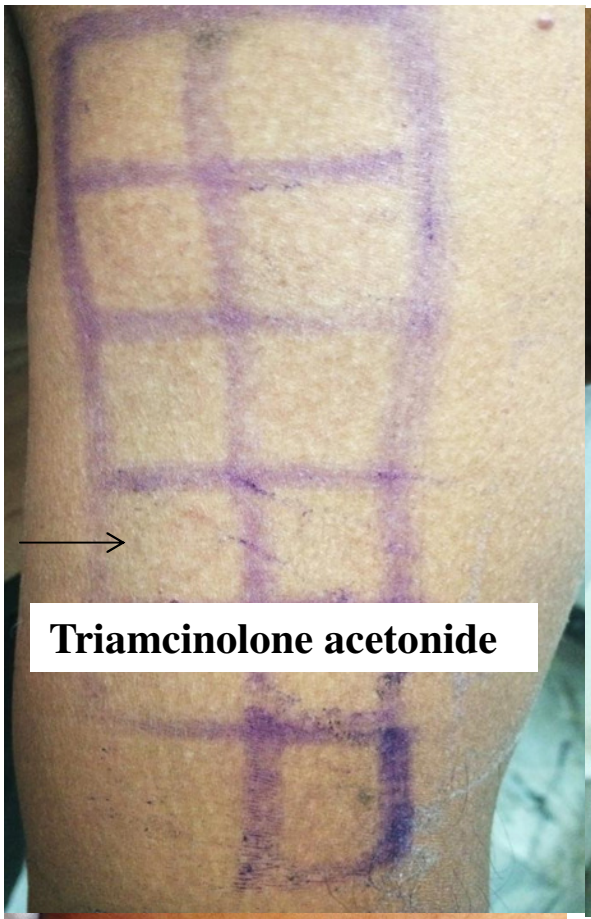


Flutivate (Pt's own)



Flutivate (Pt's own)

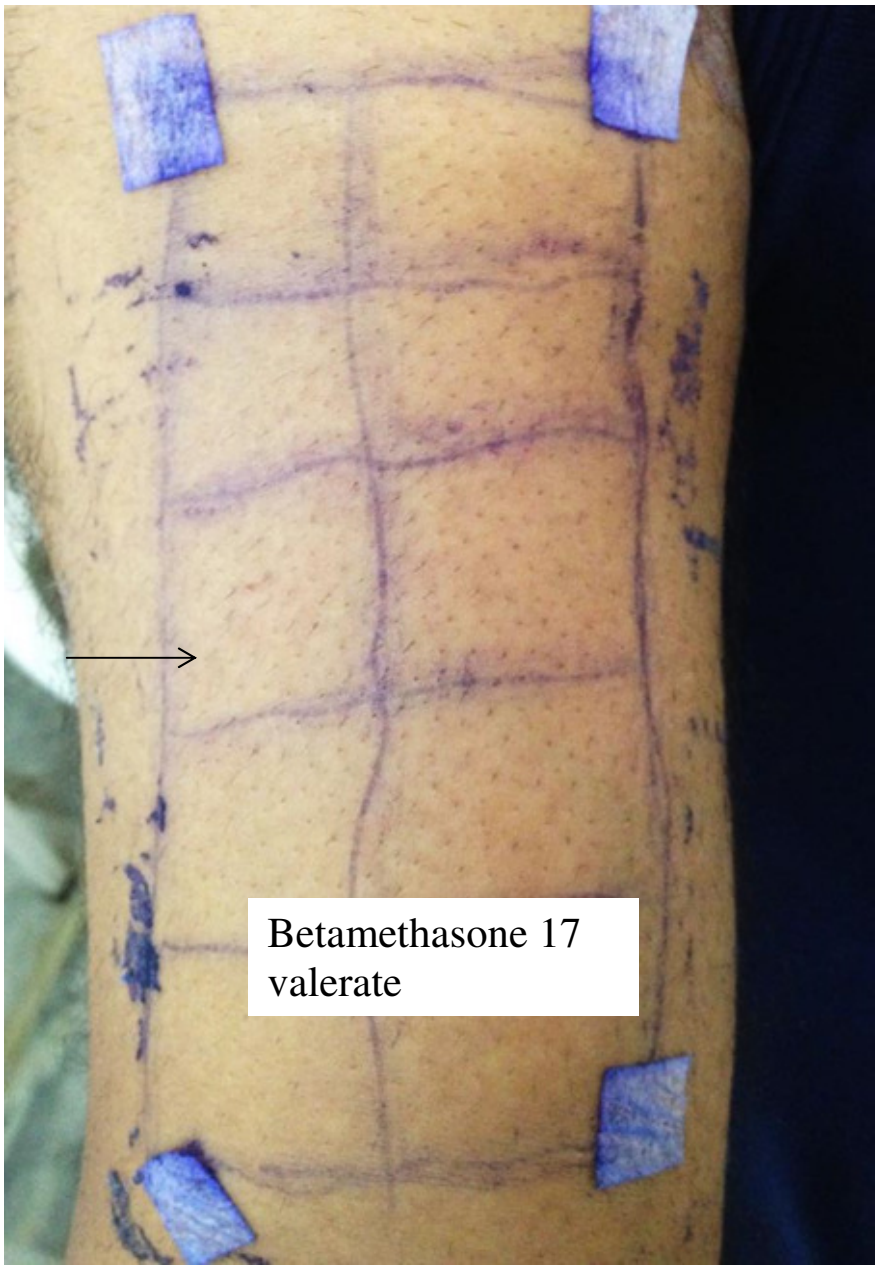
Day 3



Day5

Day 7

52 year old male who presented with perianal dermatitis of long duration who was treated with steroids and combinations in past which initially responded and now aggravated. He tested positive to triamcinolone acetonide in the corticosteroid series


Betamethasone 17
valerate

ISS (if required)

Steroid series

Steroid series +pt's own

LIST OF ANTIGENS IN CHEMOTECHNIQUE SERIES USED FOR PATCH TESTING

Sl.No.	name	age	sex	hosp.no	address -	duration	topical st	steroid us
1	rangaraj	61	M	13/07605	Pollachi	12	diprovate	1
2	bakthava	68	M	04/00660	ondipudu	4	propysali	1
3	palaniam	83	F	14/00453	tirupur	4	Momate	1
4	gunaseka	55	M	14/00619	erode	4	CFT_CP	1
5	muthuku	71	M	14/03894	ariyalur	1	Tenovate	1
6	loganatha	80	M	14/04239	trichy	5	betagel	1
7	jennifer	26	F	13/01875	tirupur	3	MomatF	1
8	radhabai	81	F	04/03734	peelamed	2	Halovate	1
9	raj	39	M	14/01480	nammaka	1	Tenovate	1
10	murugesa	64	M	12/07732	Pollachi	3	Halovate	1
11	subramar	76	M	13/05934	erode	3	Flutivate	1
12	subramar	31	M	02/02565	madurai	1	Sebowas	1
13	shankar	38	M	15/01100	nammaka	2	Tenovate	1
14	kalaiselvi	39	F	05/00045	udayamp	2	Tenovate	1
15	jithinkum	27	M	12/04932	trivandru	3	Betnovat	1
16	muthuma	52	M	15/01152	salem	4	Flutivate	1
17	padmava	38	F	15/01616	coimbato	3	Halobeta	1
18	deepthi	21	F	15/02002	coimbato	2	Momate	1
19	ramesh	35	M	11/07186	erode	1	Fucibet	1
20	prem nas	48	M	15/01907	dindugal	4	Betnovat	1
21	pradeep c	34	M	14/06991	mettupala	2	Topinate	1
22	annamala	13	M	15/01900	tirupur	3	Betagel C	1
23	saritha	46	F	15/02607	vellore	4	Flutivate	1
24	kandhasv	62	M	13/01156	kandhaswa	5	Tenovate	1

emollient	antibiotic	antibiotic	combinat	poor resp	worsenin	on immu	diagnosis	contr	bude	beta
1		0	0	1	0	0	palmopla	0	0	0
1	T- bact	1	0	1	0	0	bullous p	0	0	0
1	T- bact	1	0	0	1	0	lichen sir	0	0	0
1	CFT-CP	1	1	1	0	0	perianal p	0	0	0
1		0	0	1	0	0	atopic ecz	0	0	0
1		0	0	1	0	0	atopic ecz	0	0	0
1		0	0	1	0	0	atopic de	0	0	0
1	Fusidic a	1	1	1	0	0	atopic de	0	0	0
1		0	0	1	0	0	stasis der	0	0	0
1	Betadine,	1	1	0	1	0	atopic de	0	0	0
1		0	0	1	0	0	atopic de	0	0	0
1	T-bact,Be	1	1	1	0	0	seborrhoe	0	0	0
1		0	0	1	0	0	palmopla	0	0	0
1		0	0	1	0	0	Allergic c	0	0	0
1		0	0	1	0	0	psoriasis	0	0	0
1		0	0	0	1	0	perianal c	0	0	0
1	T-Bact	1	0	1	0	0	allergic c	0	0	0
1		0	0	1	0	0	allergic c	0	0	0
1		0	0	1	0	0	hailey ha	0	0	0
1	Gentamy	1	1	1	0	0	stasis der	0	0	0
1		0	0	1	0	0	stasis der	0	0	0
1	Gentamy	1	1	1	0	0	atopic de	0	0	0
1		0	0	0	1	0	allergic c	0	0	0
1		0	0	1	0	0	stasis der	0	0	0

triamcinc	tixocorto	alclometa	clobetaso	dexameth	hydrocor	PATIENTS OWN
0	0	0	0	1	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	1	0	0	0	0	0
0	0	0	0	0	0	0
1	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	1	0	0	0	0	1-FLUTIVATE
0	0	0	0	0	0	0

BIBLIOGRAPHY

1. Hench PS, Kendall EC, Slocumb CH, Polley HF. The effect of a hormone of the adrenal cortex (17-hydroxy-11-dehydrocorticosterone:compound E) and of pituitary adrenocorticotropic hormone on rheumatic arthritis. Proc Staff Meet Mayo Clin1949;24:181
2. Sulzberger MB, Witten VH. Preliminary and short reports. The effect of topically applied compound F in selected dermatoses. J Invest Dermatol 1952;19:101–102
3. Saraswat A. Contact allergy to topical corticosteroids and sunscreens. Indian J DermatolVenereolLeprol 2012;78:552-9.
4. Lauerma A. Contact hypersensitivity to glucocorticosteroids. Am J Contact Dermat 1992;31:112–132.
5. Kooij R. Hypersensitivity to hydrocortisone. Br J Dermatol 1959;71:392–394
6. Kendall PH. Untowards effects following local hydrocortisone injection. Ann Phys Med 1958;4:170–175
7. Rietschel R. and Fowler J. (2008) Fisher's contact dermatitis (6th edition). Hamilton ont: BC Decker
8. Baeck, M., Marot, L., Nicolas, J.-F., Pilette, C., Tennstedt, D. and Goossens, A. (2009), Allergic hypersensitivity to topical and systemic corticosteroids: a review. Allergy, 64: 978–994.
9. Räsänen L, Hasan T. Allergy to systemic and intralesional corticosteroids. Br J Dermatol 1993;128:407–411.
10. Lauerma AI, Reitamo S. Allergic reactions to topical and systemic corticosteroids. Eur J Dermatol 1994;5:354–358.
11. Torres, Maria J; Canto, Gabriela Hypersensitivity Reactions to Corticosteroids.Current Opinion in Allergy & Clinical Immunology. 2010:10(4):273-279..
12. http://www.allergyclinic.co.nz/corticosteroid_allergy.aspx Vincent St Aubyn Crump Corticosteroid allergy.
13. Dooms-Goossens A, Andersen KE, Brandao FM. Corticosteroid contact allergy: an EECDRG multicentre study. Contact Dermatitis1996;35:40–44.
14. Bjarnason, B;Flosadóttir, E;Fischer, Reactivity at Edges of Corticosteroid Patch Tests May Be an Indicator of a Strong Positive Test Response Dermatology; 1999; 199, 2;130-134
15. SAINT-MEZARD, P., ROSIERES, A., KRASTEVA, M., BERARD, F., DUBOIS, B., KAISERLIAN, D., & NICOLAS, J. F Allergic contact dermatitis. European Journal of Dermatology, 2004.14(5); 284-295.
16. Frosch PJ, Menne T, Lepoitttevin J-P, eds. contact Dermatitis 4th edn.Berlin:Springer,2006:811-30

17. Martins, L. E. A. M., & Reis, V. M. S. D. (2011). Immunopathology of allergic contact dermatitis. Anaisbrasileiros de dermatologia, 86(3), 419-433.
18. Vocanson, M., Hennino, A., Rozieres, A., Poyet, G., & Nicolas, J. F. Effector and regulatory mechanisms in allergic contact dermatitis. Allergy, 2009. 64(12);1699-1714.
19. Spiewak, R. (2008). Patch testing for contact allergy and allergic contact dermatitis. Open Allergy J, 1, 42-51.
20. Davis MD, Bhate K, Rohlinger AL, Farmer SA, Richardson DM, Weaver AL. Delayed patch test reading after 5 days:The Mayo Clinic experience.J Am AcadDermatol. 2008 Aug;59(2):225-33.
21. Ghosh, S. (2006). Patch testing: broadened spectrum of indications. Indian Journal of Dermatology, 51(4), 283.
22. LuísUva, Diana Miguel, CatarinaPinheiro, et al., Mechanisms of Action of Topical Corticosteroids in Psoriasis, International Journal of Endocrinology, vol. 2012;
23. Sanjay K. Rathi, Paschal D'Souza. Rational and Ethical Use of Topical Corticosteroids Based on Safety and Efficacy Indian J Dermatol. 2012 Jul-Aug; 57(4): 251–259.
24. Lee, N. P., &Arriola, E. R. (1999). Topical corticosteroids: back to basics. Western Journal of Medicine, 171(5-6), 351.
25. Giannotti B. Current treatment guidelines for topical corticosteroids. Drugs 36:9-14.
26. Long, C. C., & Finlay, A. Y. (1991). The finger-tip unit—a new practical measure. Clinical and experimental dermatology, 16(6), 444-447.
27. Coondoo, A., Phiske, M., Verma, S., &Lahiri, K. (2014). Side-effects of topical steroids: A long overdue revisit. Indian dermatology online journal.5(4), 416.
28. Dey, V. K. (2014). Misuse of topical corticosteroids: A clinical study of adverse effects. Indian dermatology online journal,5(4), 436.
29. Rani R. Vatti, Fatima Ali, Suzanne Teuber, Christopher Chang, M. E ric Gershwin Hypersensitivity Reactions to Corticosteroids Clinical Reviews in Allergy & ImmunologyAugust 2014;Volume 47: 26-37
30. Gönül, M. and Gül, Ü. (2005), Detection of contact hypersensitivity to corticosteroids in allergic contact dermatitis patients who do not respond to topical corticosteroids. Contact Dermatitis, 53: 67–70.
31. Matura, M., Goossens, A. and Matura, M. (2000), Contact allergy to corticosteroids. Allergy, 55: 698–704
32. MarléneIsaksson; Magnus Bruze. Contact Allergen of the Year: Corticosteroids Dermatitis. 2005;16(1):3-5.
33. Lepoittevin JP, Drieghe J, Dooms-Goossens A. Studies in patients with corticosteroid contact allergy: understanding cross-reactivity among different steroids. Arch Dermatol 1995;131:31–37.

34. Baeck, M., Chemelle, J. A., Goossens, A., Nicolas, J. F. and Terreux, R. (2011), Corticosteroid cross-reactivity: clinical and molecular modelling tools. Allergy, 66: 1367–1374.

35. Jacob S.E., Steele T. Corticosteroid classes: A quick reference guide including patch test substances and cross-reactivity Journal of the American Academy of Dermatology, 2006: 54 (4), p. 723-727
36. Wilkinson, S. M. (2000), Corticosteroid cross-reactions: an alternative view. Contact Dermatitis, 42: 59–63
37. CaterinaFoti, Gianfranco Calogiuri, NicolettaCassano, RosalbaBuquicchio, Gino A Vena Contact allergy to topical corticosteroids: update and review on cross-sensitization Recent Pat Inflamm Allergy Drug Discov 2009 Jan;3(1):33-9
38. Isaksson M, Bruze M, Goossens A, Lepoittevin JP. Patch- testing with serial dilutions of tixocortolpivalate and potential cross-reactive substances. ActaDerm Venereology 2000 Jan-Feb;80(1):33-8
39. Coopman S, Degreef H, Dooms-Goossens A. Identification of cross-reaction patterns in allergic contact dermatitis from topical corticosteroids. Br J Dermatol 1989;121:27–34.
40. Isaksson M, Bruze M, Lepoittevin JP, Goossens A. Patch testing with serial dilutions of budesonide, its R and S diastereomers, and potentially cross-reacting substances. Am J Contact Dermat 2001;12:170–176.
41. Berl V, Claudel E, Gerberick G, Lepoittevin JP. Allergic contact dermatitis to corticosteroids: a mechanistic study. Contact Dermatitis2008;58:10.
42. Isaksson M, Bruze M. Corticosteroid cross reactivity. Contact Dermatitis 2003;49:53–54.
43. Hausen BM, Foussereau J. The sensitizing capacity of tixocortolpivalate. Contact Dermatitis 1988;18:63–64.
44. Wilkinson SM, Hollis S, Beck MH. Reactions to other corticosteroids in patients with allergic contact dermatitis to hydrocortisone. Br J Dermatol 1995;132:766–777.
45. Davis, M.D., el-Azhary, R.A., Farmer, S.A. Results of patch testing to a corticosteroid series: a retrospective review of 1188 patients during 6 years at Mayo Clinic. J Am AcadDermatol. 2007; 56: 921–927.
46. Baeck, M., Chemelle, J.-A., Terreux, R., Drieghe, J. and Goossens, A. (2009), Delayed hypersensitivity to corticosteroids in a series of 315 patients: clinical data and patch test results. Contact Dermatitis, 61: 163–175.
47. Dooms-Goossins, A. and Morren, M. (1992), Results of routine patch testing with corticosteroid series in 2073 patients. Contact Dermatitis, 26: 182–191.

48. Venturini M, Lobera T, Del Pozo MD, Gonzales I, Blasco A. Immediate hypersensitivity to corticosteroids. J InvestigAllergolClinImmunol 2006;16:51–
49. Posadas SJ, Pichler WJ. Delayed drug hypersensitivity reactions – new concepts. ClinExp Allergy 2007;37:989–999
50. Degreef H, Dooms-Goossens A. The new corticosteroids: are they effective and safe? DermatolTher 1993;11:155–160.
51. Lauerma AI. Occupational contact sensitization to corticosteroids. Contact Dermatitis 1998;39:328–329.
52. Kamm GL, Hagmeyer KO. Allergic type reactions to corticosteroids. Ann Pharmacother 1999;33:451–460.
53. Isaksson M, Bruze M. Corticosteroids. Dermatitis 2005;16:3–5.
54. Bennett ML, Fountain JM, McCarty MA, Sherertz EF. Contact allergy to corticosteroids in patients using inhaled or intranasal corticosteroids for allergic rhinitis or asthma. Am J Contact Dermat 2001;12:193–196.
55. Thyssen JP, Maibach HI. Drug-elicited systemic allergic (contact) dermatitis – update and possible pathomechanisms. Contact Dermatitis 2008;59:195–202.
56. Le Coz CJ. Hypersensitivity to corticosteroids. Ann DermatolVenereol 2002;129:346–347.
57. Dooms-Goossens A. Corticosteroid contact allergy: a challenge to patch testing. Am J Contact Dermat 1993;4:120–122.
58. Goh CL. Cross sensitivity to multiple topical corticosteroids. Contact Dermatitis 1989;20:65–67.
59. Rodriguez-Serna M, Silvestre JF, Quecedo E, Martinez A, Miguel FJ, Gauchia R. Corticosteroid allergy: report of 3 unusually acute cases. Contact Dermatitis 1996;35:361–362.
60. Amin N, Brancaccio R, Cohen D. Cutaneous reactions to injectable corticosteroids. Dermatitis 2006;17:143–146.
61. Wilkinson SM, English JSC. Hydrocortisone sensitivity: a prospective study of the value of tixocortolpivalate and hydrocortisone acetate as patch test markers. Contact Dermatitis 1991;25:132–133.
62. Isaksson M, Bruze M, Goossens A, Lepoittevin JP. Patch-testing with serial dilutions of tixocortolpivalate and potential cross-reactive substances. ActaDermVenereol 2000;80:33–38.
63. Isaksson M, Bruze M, Goossens A, Lepoittevin JP. Patch testing with budesonide in serial dilutions: the significance of dose, occlusion time and reading time. Contact Dermatitis 1999;40:24–31.
64. Lauerma A. Screening for corticosteroid contact sensitivity: comparison of tixocortolpivalate, hydrocortisone 17-butyrate and hydrocortisone. Contact Dermatitis 1991;24:123–130.
65. Isaksson M, Brandao FM, Bruze M, Goossens A. Recommendation to include budesonide and tixocortolpivalate in the European standard series. Contact Dermatitis 2000;43:41–63.

66. Boffa MJ, Wilkinson SM, Beck MH. Screening for corticosteroid contact hypersensitivity. Contact Dermatitis 1995;33:149–151.
67. Wilkinson SM, Beck MH. Corticosteroid contact hypersensitivity: what vehicle and concentration? Contact Dermatitis1996;34:305–308.
68. Isaksson M, Beck MH, Wilkinson SM. Comparative testing with budesonide in petrolatum and ethanol in a standard series. Contact Dermatitis 2002;47:123–
69. Isaksson M, Gruvberger B, Persson L, Bruze M. Stability of corticosteroid patch test preparations. Contact Dermatitis2000;42:144–148.
70. Isaksson M, Bruze M. Late patch-test reactions to budesonide need not be a sign of sensitization induced by the test procedure. Am J Contact Dermat 2003;14:154–156.
71. Isaksson M, Bruze M, Björkner B, Hindsen M, Svensson L. The benefit of patch testing with a corticosteroid at a low concentration.Am J Contact Dermat 1999;10:31–33.
72. Isaksson M, Bruze M, Matura M, Goossens A. Patch testing with low concentrations of budesonide detects contact allergy. Contact Dermatitis 1997;37:241–242.
73. Isaksson M. Corticosteroid contact allergy – the importance of late readings and testing with corticosteroids used by the patients.Contact Dermatitis 2007;56:56–57.
74. Weber F, Barbaud A, Reichert-Penetrat S, Danchin A, Schmutz JL. Unusual clinical presentation in a case of contact dermatitis due to corticosteroids diagnosed by ROAT. Contact Dermatitis 2001;44:105–106.
75. Seukeran DC, Wilkinson SM, Beck MH. Patch testing to detect corticosteroid allergy: is it adequate? Contact Dermatitis1997;36:127–130.
76. Wilkinson SM, English JS. Patch tests are poor detectors of corticosteroid allergy. Contact Dermatitis 1992;26:67–68.
77. Mimesh S, Pratt M. Allergic contact dermatitis from corticosteroids: reproductibility of patch testing and correlation with intradermal testing. Dermatitis 2006;17:137–142.
78. Aberer W, Bircher A, Romano A, Blanca M, Campi P, Fernandez J et al. Drug provocation testing in the diagnosis of drug hypersensitivity reactions: general considerations. Allergy 2003;58:854–863.
79. Coloe J, Zirwas M. Allergens in corticosteroid vehicles. Dermatitis 2008;19:38–42
80. Buettiker U, Keller M, Picheler WJ, Braathen LR, Yamalkar N. Oral prednisolone induced acute generalized exanthematouspustulosis due to corticosteroids of group A confirmed by epicutaneous testing and lymphocyte transformation tests. Dermatology2006;213:40–43.

81. Comaish S. A case of hypersensitivity to corticosteroids. Br J Dermatol 1969;81:919–925.
82. Wilkinson SM, English JSC, Mattey DL. In vitro evidence of delayed-type hypersensitivity to hydrocortisone. Contact Dermatitis1993;29:241–245.
83. Braathen SR, Thorsby E. Human epidermal Langerhans cells are more potent than blood monocytes in inducing some antigen-specific T cell responses. Br J Dermatol 1983;108:139–146.
84. Lauerma A, Rasanen L, Reunala T, Reitamo S. Langerhans cells but not monocytes are capable of antigen presentation in vitro in corticosteroid contact hypersensitivity. Br J Dermatol 1990;123:699–705.
85. Ebo D, Dombrecht E, Bridts C, Aerts N, De Clerck L, Stevens W. Combined analysis of intracellular signalling and immunophenotype of human peripheral blood basophils by flow cytometry: a proof of concept. ClinExp Allergy 2007;37:1668–
86. Bundgaard H. The possible implication of steroid-glyoxal degradation products in allergic reactions to corticosteroids. Arch Pharm Chem 1980;8:83–90.
87. Matura M., Lepoittevin JP, Arbez-Gindre C, Goossens A. Testing with corticosteroid aldehydes in corticosensitive subjects (preliminary results). Contact Dermatitis 1998;38:106–108.
88. Dooms-Goossens A. Is there a relationship between contact allergy to alcohols and contact allergy to corticosteroids? Eur J Dermatol 1993;3:713.
89. Kuligowski ME, Chang A, Van Baar H. Contact allergy to alcohols with coexisting hypersensitivity to corticosteroids. Eur J Dermatol1993;3:183–186.
90. Wilkinson SM, Jones MF. Corticosteroid usage and binding to arginine. Determinants of corticosteroid hypersensitivity. Br J Dermatol1996;135:225–230.
91. Dooms-Goossens A, Lepoittevin JP. Studies on the contact allergenic potential of mometasonefuroate: a clinical and molecular study. Eur J Dermatol 1996;6:339–340.
92. Schoenmakers A, Vermorken A, Degreef H, Dooms-Goossens A. Corticosteroid or steroid allergy? Dermatitis 1992;26:159–162.
93. Block H, Holliday AK. Modern physical chemistry. London: Butterworths, 1973.
94. Isaksson M. Systemic contact allergy to corticosteroids revisited. Contact Dermatitis 2007;57:386–388.
95. Srinivas CR, Lakshmi C. Principles of topical therapy in dermatology. In: Valia RG, Valia AR, editors. IADVL Textbook of Dermatology. 3rd ed., Vol. 2. Mumbai, India: Bhalani Publishing House; 2008. p. 1591-618.

96. Wolverton SE. Topical Corticosteroids. Comprehensive Dermatologic Drug Therapy. 2nd ed. Philadelphia USA: Saunders Elsevier; 2007. p. 595-624.
97. Giuliana Carlos, Pablo Uribe, Pablo Fernández-Peñas. Rational use of topical corticosteroids. AustPrescr 2013;36:159-61
98. Verma SB, Hay R. Topical steroid induced tineapseudoimbricata: A striking form of tinea incognito [Accepted for publication Int J Dermatol 2014].
99. Kuflik JH, Schwartz RA. Acneiform eruptions. Cutis 2000;66:97-100. 14. Momin S, Peterson A, Del Rosso JQ.
100. Drug-induced acneformeruptions:Definitions and causes. CosmetDermatol 2009;22:28-37.
101. Goossens A, Huygens S, Matura M, Degreef H. Fluticasone propionate: a rare contact sensitizer. Eur J Dermatol 2001;11:29–34.
102. Akiba H, et al. Skin inflammation during contact hypersensitivity is mediated by early recruitment of CD8+ T cytotoxic 1 cells inducing keratinocyte apoptosis. J Immunol2002; 168: 3079-87.
103. Menne T. Prevention of nickel allergy by regulation of specific exposures. Ann Clin Lab Sci1996; 26: 133-8.
104. Schnuch A, Geier J, Lessmann H, Uter W. Decrease in nickel sensitization in young patients--successful intervention through nickel exposure regulation? Results of IVDK, 1992-2001. Hautarzt2003; 54: 626-32.
105. Lepoittevin J, Leblond I. Hapten-peptide T cell receptor interac- tions: molecular basis for the recognition of haptens by T lympho- cytes. Eur J Dermatol1997; 7: 151-4.
106. Dupuis GB. Nature of hapten-protein interactions. Chemically reactive function in haptens and proteins, in allergic contact dermatitis to simple chemicals. A molecular approach. New-York: Ed Marcel Dekker, Inc.: 1982.
107. Corazza M, Mantovani L, Maranini C, Bacilieri S, Virgili A. Contact sensitization to corticosteroids: increased risk in long term dermatoses. Eur J Dermatol2000; 10: 533-5.
108. Berard F, Marty JP, Nicolas JF. Allergen penetration through the skin. Eur J Dermatol2003; 13: 324-30.
109. Rocha N, Silva E, Horta M, Massa A. Contact allergy to topical corticosteroids 1995-2001. Contact Dermatitis 2002; 47
110. Wattanakrai P, Temnithokul B, Pootongkam S, Pattern of corticosteroid allergy in Thailand. Dermatitis 2010; 21:203-6

ABBREVIATIONS

CS- CorticoSteroids

TCS- Topical corticoSteroids

CD - Contact dermatitis

ICD - Irritant contact dermatitis

ACD- Allergic Contact Dermatitis

DTH- Delayed type hypersensitivity

Ig–Immunoglobulins

CD-Cluster of Differentiation

h - hours (in relation to reading of patch test)

ICDRG - International Contact Dermatitis Research Group

DC - Dendritic cells

LCs- Langerhans cells

APCs- Antigen presenting cells

IL- Interleukins

IFN- Interferons

TNF- Tumor necrosis factor

Pts- Patients

ROAT- Repeated open application test

HPA-Hypothalamo pitutary axis

FTU-Finger Tip Unit

OH-Hydroxal

Master chart codes – o – Negative 1-Positive

ஒப்பதல் படிவம்

தேதி

அகிலா க. ஆகிய நான் PSG மருத்துவக்கல்லூரியின் **தோல் பால்வினை மற்றும் தொழுநோய்** துறையின் கீழ் **"சருமத்தில் ஏற்படும் அரிப்பு நோய்க்கு நீண்ட நாட்கள் ஸ்டீராய்டு எனும் மருந்து தடவியும் குணமடையாத நோயாளிகளுக்கு எவ்வகை ஸ்டீராய்டு மருந்துகளுக்கு ஒவ்வாவை உள்ளது என்று முதுகில் ஒட்டிப்பார்க்கும் ஒவ்வாமை கண்டறியும் பரிசோதனை"** என்ற தலைப்பில் ஆய்வு மேற்கொள்ள உள்ளேன்

என் ஆய்வு வழிகாட்டி : மரு. சி.ஆர் ஸ்ரீனிவாஸ்

ஆய்வு மேற்கொள்வதற்கான அடிப்படை

சரும அரிப்பு நோய்க்கு மருந்தாக உபயோகப்படுத்தபடும் ஸ்டீராய்டுக்கு ஒவ்வாமை இருப்பின் சிறந்த முறையில் அரிப்பு நோயை குணப்படுத்த முடியாது.

ஆய்வின் நோக்கம்

இந்த ஆய்வின் மூலம் அவ்வொவ்வாமை பொருட்களை தவிர்ப்பதால் சிறந்த முறையில் சரும அரிப்பு நோயை குணப்படுத்த முடியும்.

ஆய்வில் பங்கு பெறும் நபர்களின் எண்ணிக்கை : 30 நபர்கள்

ஆய்வு மேற்கொள்ளும் இடம் : பி.எஸ்.ஜி மருத்துவமனை,
தோல் பால்வினை மற்றும் தொழுநோய் துறை

ஆய்வின் பலன்கள் :

ஸ்டீராய்டு ஒவ்வாமை அறிந்து கொண்டு அவற்றை தவிர்க்கலாம்.

ஆய்வினால் ஏற்படும் அசௌகரியங்கள் / பக்க விளைவுகள் :

இப்பரிசோதனையின் பொழுது ஒரு சிலருக்கு அரிப்பு ஏற்பட வாய்ப்பு உள்ளது. அதுவும் மூன்று நாட்கள் மருந்து உட்கொள்ளுதல் மூலமாக குணமடையும்.

இந்த ஆய்வில் கிடைக்கும் தகவல்கள் 10 வருடங்கள் பாதுகாக்கப்படும். இவை வேறு எந்த ஆய்விற்கும் பயன்படுத்தப்பட மாட்டாது. எந்த நிலையிலும் உங்களைப் பற்றிய தகவல்கள் யாருக்கும் தெரிவிக்கப்பட மாட்டாது. இவை இரகசியமாக வைக்கப்படும்.

இந்த ஆய்வில் பங்கேற்க ஒப்புக் கொள்ளுவதால் எந்தவிதமான பலனும் உங்களுக்கு கிடைக்காது. எந்த நேரத்தில் வேண்டுமானாலும் ஆய்விலிருந்து விலகிக் கொள்ளும் உரிமை உங்களுக்கு உண்டு. ஆய்விலிருந்து விலகிக் கொள்வதால் உங்களுக்கு அளிக்கப்படும் சிகிச்சையில் எந்த வித மாற்றமும் இருக்காது.

இந்த ஆராய்ச்சிக்காக உங்களிடம் சில கேள்விகள் கேட்கப்படும் / சில இரத்த மாதிரிகள் அல்லது திசு மாதிரிகள் எடுக்கப்படும்.

மேலும் இந்த ஆய்வில் பங்கு கொள்வது உங்கள் சொந்த விருப்பம். இதில் எந்த விதக் கட்டாயமும் இல்லை. நீங்கள் விருப்பப்பட்டால் இந்த ஆய்வின் முடிவுகள் உங்களுக்குத் தெரியப் படுத்தப்படும்.

ஆய்வாளரின் கையொப்பம் :

தேதி :

ஆய்வுக்குட்படுபவரின் ஒப்புதல்

நான் இந்த ஆராய்ச்சியின் நோக்கம் மற்றும் அதன் பயன் பாட்டினைப் பற்றி தெளிவாகவும் விளக்கமாகவும் தெரியப்படுத்தப்பட்டுள்ளேன். இந்த ஆராய்ச்சியில் பங்கு கொள்ளவும் இந்த ஆராய்ச்சியின் மருத்துவ ரீதியான குறிப்புகளை வரும் காலத்திலும் உபயோகப்படுத்திக் கொள்ளவும் முழு மனதுடன் சம்மதிக்கிறேன்.

ஆய்வுக்குட்படுபவரின் பெயர், முகவரி :

கையொப்பம் :

தேதி :

ஆய்வாளரின் தொலைபேசி எண் 9597484444

மனித நெறிமுறைக் குழு அலுவலகத்தின் தொலைபேசி எண். 0422-2570170 Extn. 5818

PSG Institute of Medical Science and Research, Coimbatore

INFORMED CONSENT

I , AKILA.K , am carrying out a study on the topic: PATCH TESTING TO DETECT CONTACT HYPERSENSITIVITY TO TOPICAL CORTICOSTEROIDS

as part of my research project being carried out under the aegis of the Department of: DERMATOLOGY VENEROLOGY & LEPROLOGY

My research guide is: Dr. C.R.SRINIVAS.

The justification for this study is:

Topical steroids are the most important therapy used in allergic contact dermatitis (ACD),atopic dermatitis,stasis dermatitis etc.,. But contact sensitivity from steroids themselves is becoming increasingly reported in the past decade. It should be suspected, especially, if there is no response to steroid therapy or worsening in the pre-existing lesions. Knowledge of allergen will enable the patient to receive appropriate treatment which will improve their dermatitis. Diagnosis is best done by patch testing which is read on 48hrs, 5^{th} and 7^{th} day

The objectives of this study are:

Primary Objective:

To study the contact hypersensitivity of patients to topical steroids who do not respond to topical corticosteroids in allergic contact dermatitis patients.

Secondary Objective:

To find the prevalence of contact hypersensitivity to topical corticosteroids in allergic contact dermatitis patients attending our OPD and provide a allergen free alternative medicament

Study participants: Patients with
All patients attending our dermatology out- patient department-males/females, with history of topical steroid application, who do not respond to /or aggravate with topical corticosteroids.

Location: PSGIMS & R
We request you to kindly cooperate with us in this study. We propose to collect background information and other relevant details related to this study. We will be carrying out:

Initial interview (specify approximate duration): 15 minutes.

Data collected will be stored for a period of 10 years. We will not use the data as part of another study.

Clinical examination will be done to assess if any active lesions are present in the body.

Procedure:
Patch test will be done on the upper back using Finn Chambers with the cosmetic series .Grading is according to International Contact Dermatitis Research Group(ICDRG) scale day 3 , day 5 and day7.The patch test area should not be washed until day 3,should not be exposed to sunlight.

Benefits from this study: Knowledge of allergen will enable to find the suitable topical corticosteroid preparations devoid of the allergen which will improve their dermatitis.

Risks involved by participating in the study: will develop small allergic reaction over back which can be treated by taking antihistamines for 3days.

How the **results** will be used:
Based on these results patch testing is non invasive and simple procedure to detect contact hypersensitivity to topical corticosteroids.

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the PI with date: Witness:

Contact number of PI: 9597484444

Contact number of Ethics Committee Office: 0422 2570170 Extn.: 5818

PATIENT INFORMATION SHEET:

1. Demographics
2. Complaints with duration
3. Seasonal variation H/o atopy
4. Site involved
5. Erythema/Vesicles/Oozing/Pustules/Scaling/Depigmentation/Purpura/ Lichenification
6. History of any other skin disorder
7. History of systemic illness
8. History of treatment for the skin lesions with duration- topical or systemic - steroids, antibiotics, antifungal, others. If so details of the same – name and brand
9. How long did he/she use the topical steroids?
10. Was he/she applying it regularly or irregularly?
11. If irregular how many days he/she did not apply
12. Is he/she on oral steroids or other immunosuppressants?
13. Probable diagnosis:

CORTICOSTEROID SERIES

S.NO	ANTIGEN	%	DAY		
			3	5	7
01	Control				
02	Budesonide	0.01			
03	Betamethasone-17-valerate	1			
04	Triamcinolone acetonide	1			
05	Tixocortol-21-pivalate	0.1			
06	Aclolometasone-17,21-dipropionate	1			
07	Clobetasole 17 propionate	1			
08	Dexamethazone-21-phosphate disodium salt	1			
09	Hydrocortisone-17-butyrate	1			

PATIENTS OWN: